OCT 20 1919

Vol. III. No. 3. Serial No. 11. *July-Sept., 1919*

ENDOCRINOLOGY

The BULLETIN of the ASSOCIATION for the STUDY of

INTERNAL SECRETIONS

CONTENTS

REMARKS ON THE FUNCTIONS OF THE SUPRARENAL GLANDS AS REVEALED BY CLINICAL PATHOLOGICAL STUDIES OF HUMAN BEINGS AND BY EXPERIMENTS ON ANIMALS. By Lewellys F. Barker, Baltimore 253

FETAL AND MATERNAL ATHYROSIS. II. By G. Ennis Smith, London, Canada 262

DIABETES IN INFANCY AND CHILDHOOD. By Isaac A. Abt, Chicago . . 273

THE FUNCTION OF THE THYMUS GLAND. By Eduard Uhlenhuth, New York 285

THE EFFECT OF SPLENECTOMY ON THE THYMUS. By F. C. Mann, Rochester, Minn. 299

THE FUNCTIONS OF THE INTERNAL SECRETION OF THE PLACENTA. By Frederick S. Hammett, Philadelphia 307

THE INFLUENCE OF THE THYROID GLAND ON THE FORMATION OF ANTIBODIES. By J. Koopman, The Hague, Holland 318

THE ACTION OF ADRENALIN ON THE KIDNEY. By Frank A. Hartman and Ross S. Lang, Toronto, Canada 321

ENDOCRINOPATHIC CONSTITUTIONS AND PATHOLOGY OF WAR. By N. Pende, Palermo, Italy 329

BOOK REVIEW:

THE INTERNAL SECRETIONS AND THE NERVOUS SYSTEM. By Dr. M. Laignel-Lavastine, Paris 342

THE LITERATURE ON THE INTERNAL SECRETIONS. Containing 284 Titles and Articles Reviewed.

Published Quarterly by the Association for the Study of Internal Secretions, 1100-1103 Title Insurance Bldg., Los Angeles, California. Subscription Rates: $5.00 a Year in Advance. Single Copies $1.50, Postpaid.

Entered as second-class matter February 5, 1917, at the post office at Los Angeles, California, under the Act of March 3, 1879.

Helps In Diagnosing

Originated and Endorsed by Prominent Physicians
Practical and Convenient

RENAL FUNCTIONATION

Phenolsulphonephthalein

ACIDOSIS CONDITIONS

Apparatus For Determining:

CO_2 Tension of Alveolar Air
Alkali Reserve of Blood
Hydrogen-Ion Concentration of Blood

UREA IN URINE AND IN BLOOD

Urease-Dunning

Literature Upon Request

Hynson, Westcott & Dunning
BALTIMORE

ENDOCRINOLOGY

THE BULLETIN of the ASSOCIATION for the STUDY of

INTERNAL SECRETIONS

JULY-SEPTEMBER, 1919

REMARKS ON THE FUNCTIONS OF THE SUPRARENAL GLANDS AS REVEALED BY CLINICAL-PATHOLOGICAL STUDIES OF HUMAN BEINGS AND BY EXPERIMENTS ON ANIMALS.*

Lewellys F. Barker, M.D.

Johns Hopkins Hospital, Baltimore.

The Association for the Study of the Internal Secretions has been organized and its journal, Endocrinology, is being published in the interests both of the advance of science and of better medical practice. Our objects include not only the further development of a pure science of endocrinology, but also the evolution of an applied science of endocrinology and the improvement of the medical art as far as it is exercised in endocrine domains. The membership of our Association includes therefore not only investigators and teachers in the pre-clinical medical sciences of anatomy, histology, embryology, physiology, physiological chemistry, pharmacology and experimental pathology, but also many representatives of the clinical sciences of diagnosis and therapy and of the closely allied sciences of pathological anatomy and pathological physiology. Only through the mutual respect, the thorough reciprocal understanding and the closest co-operation in every way of workers in all these sciences can

*Address of the President of the Association for the Study of Internal Secretions, Atlantic City Meeting, June 9th, 1919.

progress in knowledge of the internal secretions and utilization of it best be made. It is hoped and believed that the Association and its journal may go far toward stimulating research in clinics as well as in laboratories and toward co-ordinating the interests of the workers in all subdivisions of the endocrine field.

No better example of the value of correlation of the activities of endocrine investigators of different sorts could, perhaps, be given than that offered by a consideration of studies in the functions of the suprarenal glands in health and in disease; and at this meeting, at which it is my privilege to preside, it is to this subject that I desire to refer. From the time of the great clinician Addison to the present, practising physicians have been deeply interested in the normal and abnormal functioning of the suprarenals, and with the rise of laboratory research a goodly number of scientists have busied themselves with researches bearing upon the structure and functions of these mysterious organs. You will recall that the president of this association last year took one phase of the subject into careful consideration, and a glance at the several quarterly issues of our journal shows how widespread throughout the world and among different types of investigators is the interest in, and how painstaking is the research at present going on in attempts to elucidate, the influences of these glands upon other parts of the body under normal conditions and in pathological states. That out of the studies already made and those that will be conducted in the near future, when they are properly co-ordinated, much will emerge that will illuminate an area hitherto dark and obscure, no physician with vision can doubt. Though we know but little as yet in comparison with what there is still to be learned about the suprarenal glands, the contributions that have been made and that are now being made give us every reason to hope that ere long the secrets of these organs will, by a band of earnest workers, be wrested from nature.

The advantages for the study of the suprarenals derivable from division of labor in the clinical and preclinical medical sciences lie especially in the variety of the backgrounds of the workers in the several sciences, in the differences in the problems they set out to solve, and in the modes of approaching the solution of these problems by means of practical-technical procedures of different kinds. The anatomical group, the physiological-

pharmacological group, the experimental pathological group, and the clinical group of workers have different kinds of past experiences to draw upon, different materials to occupy themselves with, a different body of principles to guide them, a different set of technical methods to employ, different interests to stimulate them, and different purposes to achieve. In the end, their activities and results, when co-ordinated, converge; for all make use of the general method of science, and each contributes to knowledge that can be used by all. Thus the special desires, the special ideas, and the special activities of the single workers can ultimately be fused in the service of the emotions, the ideas and the purposes of endocrinologists in common.

Certain very stimulating ideas regarding the significance of the suprarenal glands have come, as everyone will admit, from observation at the bedside of sick human beings, and in the post-mortem room. Thus, when Addison observed that certain patients manifested profound asthenia, marked disturbances of digestion, and a peculiar bronzing of the skin, and that in their bodies, after death, there was extensive chronic disease and destruction of the suprarenal glands, the first great step toward the recognition of the significance of these structures was made. Clinicians and pathologists since Addison's time have done much to elaborate the syndrome he first observed and to enlarge our ideas of the pathological changes that may underlie it, and of its etiology. On the clinical side there are many special observations upon the motor asthenia (affecting both the voluntary muscles and the heart muscle), the low blood pressure, the anorexia, nausea, vomiting and diarrhoea, the tendency to fainting spells, the pigmentation of the skin and mucous membranes, the white line phenomenon, the anaemia, the oliguria, the slowing of the metabolic processes, the hypothermia, and the lowered resistance to infections. In some cases there was obesity, in others emaciation. In addition, clinicians have studied certain syndromes that more or less closely resemble the symptom-complex of Addison's disease, but are not identical with it—syndromes that may be met with in infancy and childhood, in adolescence, in middle life or in old age, syndromes that sometimes develop slowly, sometimes acutely. On the pathological side many special observations have also been made on the bodies of patients dead of Addison's disease or of diseases, chronic or

acute, resembling it. The frequency of tuberculous lesions of the suprarenals in such cases was early recognized, and the occasional occurrence of cancerous disease and of diffuse fibrosis of these glands was described. In some instances, no changes could be recognized in the suprarenal glands themselves, but lesions involving the nerves that supplied them were discovered. In still other cases, neither the glands nor their nerves showed any recognizable changes, and a functional disorder of the glands secondary to diseases elsewhere in the body had to be assumed to have existed. After the doctrine of internal secretions developed and it was believed that the suprarenal glands belong among the endocrine organs, it was natural for clinicians to advance the hypothesis that the symptoms of Addison's disease in which the glands were slowly destroyed were due to insufficiency of the internal secretions of these glands—to a hypo-suprarenalism (or hypoadrenia), and that in conditions resembling but not identical with Addison's disease there was also a greater or less degree of suprarenal insufficiency or hypofunction. As a result of this conception there has been, on the one hand, much speculation as to the possible causes of the hypofunction in instances in which no organic changes in the suprarenals could be found, and, on the other, an attempt favorably to influence the course of Addison's disease and of allied conditions by the institution of substitutive organo-therapy of different sorts. Another very important idea that emanated from clinical-pathological observations is that of a connection between the function of the suprarenal glands and the development, and behavior during life, of the secondary sex characters. Thus clinicians and pathologists have observed that in association with certain diseases (especially tumors) of the suprarenal glands, or of aberrant masses of suprarenal tissue in other organs, peculiar disturbances in sex domains may be met with. For example, if the disease be present in the foetus, and the child live, the condition of pseudo-hermaphroditism is prone to develop, the individual presenting to a greater or less extent the external habitus and the external genitalia of one sex though the primary sex organs (testes or ovaries) are those of the opposite sex. Or, if the disease be a little later in its development, the external and internal genitalia may be in accord, but the child matures too soon (*pubertas praecox*), a little girl of 2, 3 or 4 years of age perhaps, presenting the sexual

appearances of a girl of 14 (pubic and axillary hairs, mammary development, menstrual flow, adolescent psyche), or a boy of 6 or 7 may exhibit the somatic and psychic sexual phenomena of a boy in his teens. Or, again, should the disease develop still later in life, the body may become slowly or quickly covered by an abundant growth of hair (*hirsutismus*) and in the case of a female, in addition to the hirsutism of the trunk and extremities, and the growth of a beard and moustache upon the face, the patient may present somatic and psychic asthenic features resembling those of the male (large clitoris, great muscular power, masculine voice, love of hard labor, etc.), a condition known in clinical papers as *virilismus*. Since this sthenic condition contrasts strongly with the asthenia or adynamia that characterizes Addison's disease, in which the suprarenal glands are, as a whole, slowly destroyed, it was natural for clinicians to think of virilismus (and the allied conditions—hirsutism, premature puberty and pseudo-hermaphroditism) as examples of overactivity or hyperfunction of the suprarenal glands, though the terms hypersuprarenalism and hyperadrenia, when they have been used at all, have been applied in a different way, and perhaps less justifiably, namely, to conditions in which the blood pressure is increased. Clinical observations then, controlled by pathological-anatomical examinations made after death or after operations upon the living, have yielded these two great conceptions: (1) the conception of a loss or diminution of the function of the suprarenal glands characterized by the Addisonian syndrome, and (2) the conception of an overactivity of these glands characterized, according to the time at which the overactivity appears, by pseudo-hermaphroditism, by precocious puberty or by virilism.

Before considering further the bearing of clinical-pathological observations upon the functions of the suprarenals, let us recount some of the more important contributions of pre-clinical scientists, working in experimental laboratories, to our understanding of the nature and activities of these organs. First of all, the anatomists and histologists showed us that each human suprarenal gland is divisible into two parts, cortex and medulla, which differ from one another entirely in their morphological appearances, and which, therefore, presumably, have entirely different functions. The cells themselves, as well as the way

they are arranged, are wholly different in the cortex from those in the medulla. The medullary cells closely resemble certain cells found along the sympathetic trunks, along the aorta, and in the carotid glands; they show an especial affinity for compounds of chromium, and are accordingly known as chromophile cells. Indeed, it is believed that the medulla of the suprarenal gland is only a part of a much larger anatomical-physiological system of cells, now known as the chromaffine system. So firmly accepted is this conception of the identity of the widely distributed chromophile cells that what is proven to be true of one portion of the chromaffine system is now likely to be assumed to be true of all the other portions of this system, though strange to say many investigators, who should be familiar with the total extent of the chromaffine system, seem, when writing of suprarenal function, to forget that there is a considerable body of chromaffine tissue outside of, and even far distant from, the suprarenal glands. A second important laboratory contribution that goes far toward confirming the views just mentioned of a totally different structure and function for cortex and medulla respectively has been made by the embryologists and comparative anatomists who have demonstrated (1) that in human beings and higher animals generally the medulla of the suprarenal is derived from the *Anlage* of the sympathetic nervous system, whereas the cortex of the suprarenal has an entirely different genesis, being derived from the germ epithelium, and (2) that what correspond to cortex and medulla of the suprarenal of higher forms are in lower vertebrate forms not even spatially associated, but exist as parts of two anatomically separate and independent series of organs—the one a part of the so-called interrenal system of organs, the other as a part of the chromaffine system. Thus, in the eel, what corresponds to cortex or interrenal system includes the corpuscles of Stannius and Giacomini's mass in the pronephros. Even in man it has been found that small masses of accessory interrenal cells ("suprarenal rests") may be met with in the kidneys and at various sites within the abdomen and pelvis, though by far the majority of cells of interrenal origin in man and higher vertebrates are included in the suprarenal cortex. A third important contribution made by laboratory experiment was the bringing of the proof that the functions of the interrenal system are necessary for life and

that the death of a higher animal that is due to total extirpation of the adrenals must be the result of removal of the interrenal portion (cortex) rather than of the removal of the chromaffine portion (medulla) of these organs; it would seem that though there is enough chromaffine tissue outside of the suprarenal glands to maintain life (if, and we are not yet sure of this, the functions of the chromaffine system are essential to life) there is not enough interrenal tissue outside the suprarenals to maintain life after the suprarenal cortex has been extirpated. A fourth discovery of great significance was that of Schafer, who demonstrated that extracts of the suprarenal glands when injected cause a rise in blood pressure. And a fifth fundamental laboratory contribution was the demonstration that this blood-pressure-raising substance is derived from the chromaffine part (medulla), not from the interrenal part (cortex), and that it is a well-defined substance (adrenalin of Takamine; epinephrin of Abel) the chemical constitution of which has been determined, and methods for its artificial manufacture worked out. A sixth laboratory discovery that may prove to be of real importance is the isolation by Voegtlin and Macht of a pressor substance, not epinephrin, from the suprarenal cortex; this substance and the abundance of lipoid substances present in the cortex require study.

Coincident with and following upon these several fundamental findings by laboratory workers began a series of experiments further to determine the functions of the medulla of the suprarenal and the epinephrin it produces. A period of intensive experimental research yielded results that served as materials out of which various hypotheses concerning the significance of the suprarenals were constructed. Among the better known of these attempts at generalization are what are known as (1) the *tonus theory,* which assumes that epinephrin maintains in one way or another constantly a state of tonus in smooth muscle innervated by the sympathetic nervous system; (2) the *emergency theory,* which regards the suprarenals as an apparatus for discharging epinephrin in emergencies only; (3) the *antitoxic theory,* according to which suprarenal products neutralize poisons; or its variation, which assumes that the suprarenal products themselves are detoxicated substances; and (4) the *metabolic theory;* which postulates that the presence of minute quantities of

epinephrin are necessary for the metabolic activities of the tissues, including the oxygenation of the blood. Thus the results of experiments led to the formulation of hypotheses, which in turn stimulated further research.

These speculations have really had a heuristic effect, for groups of experimental workers have undertaken investigations in laboratories to corroborate or to refute them, and as results of their studies many important discoveries can be recorded. Thus we now possess valuable information regarding (1) the quantity of epinephrin present in the suprarenals, in other chromaffine tissues, in the various organs, and in the blood, under certain conditions; (2) the circumstances (pain, asphyxia, excitement) in which epinephrin is discharged into the suprarenal veins; (3) the influence of epinephrin (a) on the body as a whole, after subcutaneous injection, (b) on perfused organs like the heart, the spleen and the kidney, (c) on strips of muscle like that of the uterus, the intestine, the iris, the bronchial musculature and the bundle of His; (d) on the calibre of, and the blood-flow through, arteries, veins and capillaries in different regions of the body; (e) on the functions of nerves and of neuronal synapses; (f) on the content of the blood in its different varieties of white corpuscles; (g) on the discharge of red blood corpuscles from the sinuses of the liver; (h) on the secretion of saliva and other digestive juices, and (i) on the mobilization of sugar and the sugar-content of the blood. Discoveries such as these show the great value of hypotheses as the groundwork of action, for the careful testing of a hypothesis, whether it be true or not, advances knowledge. John Hunter's "Don't think; try," really meant, "Think, but do not stop at thinking; test your thought by trial." Clinicians and pathologists, to-day, are making their observations and their classifications of disease of the suprarenal glands in the light of all this new knowledge. They, too, are speculating regarding the significance of their observations at the bedside and are subjecting their hypotheses to tests by means of experimental methods carried on during the life of patients and by means of histological and chemical studies of the dead. I need refer only to (1) the use of epinephrin in the treatment of asthma, of urticaria, and of angio-neurotic oedema, (2) the administration of suprarenal gland in Addison's disease, and in other states of asthenia, hypotension, and

hypothermia, (3) the clinical conceptions of the chromaffinopathies and the interrenopathies and their subdivisions of hyperfunction, hypofunction and dysfunction, and (4) the Loewi test and the Goetsch test in clinical diagnosis, to recall to your minds some of the directions in which physicians are speculating and working in the hope of advancing knowledge in the clinical sciences of diagnosis and therapy. Real progress is here certainly being made. Though many of the hypotheses now held will later be discarded and some of the classifications will doubtless have to be revised, still these hypotheses and classifications will have served their purpose if they have stimulated closer observation and continuous experimentation, and have been regarded merely as stepping-stones in the path of progress. Clinicians and pathologists, as well as physiologists, have the right to speculate, provided their speculations are based upon the facts that have already been accumulated, and provided also that they persist in subjecting their speculations to rigid tests by further observation and experimentation.

Time will not permit me further to elaborate the topic in this brief address. But enough has perhaps been said to justify the optimism that exists among those who, both in the pre-clinical and the clinical sciences, are absorbingly occupied with the study of the suprarenal glands.

FETAL AND MATERNAL ATHYROSIS. II.

G. Ennis Smith
Institute of Public Health, Western University, London, Canada.

INTRODUCTION

The author has described a thyroid disturbance (1) that is prevalent among new-born domestic animals in western sections of this continent. The disease is one which affects swine, sheep, cattle, horses, goats and dogs, and occurs among such a wide range of animals that it appears very probable that if human beings were subjected to the same relative conditions a more or less severe form of a similar thyroid disturbance would result. A profound influence of pregnancy upon the maternal thyroid, which may develop into a pathologic condition, has to some extent been recognized, but the attention has been confined mainly to the maternal organism. The manifestations of the thyroid disturbance among domestic animals show very clearly, however, that the effects are more disastrous to the fetus than to the maternal organism. It is our opinion that when this subject has been thoroughly explored many of the cases of infantile fatality and of arrested development of children which are now vaguely designated as congenital, will be found to arise from a lack of function of the fetal thyroid which may be overcome by a proper diet and conduct of the mother during the gestation period.

REVIEW OF THE THYROID DISTURBANCE OF DOMESTIC ANIMALS

The disturbance is to a large extent endemic to certain sections and appears to correspond more or less with the distribution of goitre. Many of the young are born dead, others die in an hour or two and very few live more than 24 to 36 hours. The loss in Montana alone has amounted to about one million young pigs annually. While the loss is heaviest among swine, there are numerous cases among sheep and occasional cases among horses and cattle. The symptoms in the affected animals correspond to the symptoms of myxedema and also to the symptoms occurring after extirpation of the thyroid. The most striking feature of typical specimens is the absence of hair. The hoofs are thin-walled, short, brittle, and plainly in an undeveloped

condition. The iodine content of the thyroid is extremely low and varies inversely with the severity of the malady. There is a pronounced hyperplasia of the gland with a great multiplication of the cells of the interstitial tissue. The malady is undoubtedly due to the decreased physiological activity of the fetal thyroid which the author has designated as fetal athyrosis. The evidence eliminates an infective agent as a possible factor and indicates that the cause of the malady is a nutritional deficiency caused by a lack and possibly an uneconomic use of available iodine. Pigs born in March and April are more frequently affected than those born in May and June and even in the badly affected regions the fall litters are usually normal. Diets that tend to produce rapid growth when the amount of available iodine is low appear to make the malady more severe and to exhaust the fetal thyroid of its physiologically active constituent.

Hart and Steenbock (2) have been able to produce hairless pigs experimentally with symptoms that correspond exactly to those described by the author, by feeding the pregnant sows a high protein diet, and they confirmed our conclusions that the malady can be overcome by feeding an abundant supply of iodine. They were also able to demonstrate that the maternal as well as the fetal thyroid was involved, although to a much less degree.

While the slight disturbance of the maternal thyroid does not appear to have a very distressing effect upon the mother, yet its importance must not be underestimated because if the condition is not corrected it has a very pronounced effect upon the fetus when the animal becomes pregnant again. The primary thyroid disturbance that is produced in the maternal organism during pregnancy will be designated in this paper as maternal athyrosis.

DISORDERS OF THE HAIR, NAILS AND TEETH DURING PREGNANCY

With every well-defined thyroid disturbance and after extirpation of the thyroid, disorders of these specific epidermal appendages are invariably reported. The occurrence of disorders of the teeth, nails and hair during pregnancy is widely recognized. DeLee (3) states that during pregnancy the nails are thinner and the teeth are liable to loosen and decay and he described the ultimate effect of this state upon the hair as sim-

ilar to that of fever. We believe that it is feasible to attribute the above disorders to a lack of function of the thyroid and assuming the existence of a thyroid disturbance by the manifestation of these disorders, it would indicate that there is a very wide occurrence of a more or less severe form of maternal athyrosis.

HIGH PROTEIN METABOLISM DURING PREGNANCY

It has been pointed out that the diets that produce rapid growth tend to exhaust the fetal thyroid of its active secretion (1) and that Hart and Steenbock (2) were able to produce hairless pigs experimentally by feeding a high protein diet. It is also well known that thyroidectomy is more disastrous to carnivora than to herbivora. The above evidence indicates that any increase in the protein metabolism requires a corresponding increase in the thyroid activity. If there is not an abundant supply of iodine the thyroid will eventually become exhausted, and with the low iodine concentration of the blood the thyroid will attempt to accommodate itself to that condition and hyperplasia will take place. This was actually the condition found with the hairless pigs. The iodine content of the fetal thyroid was reduced to a mere trace and the size of the gland was increased tenfold and to a less degree the maternal thyroid was similarly affected.

The proteolytic enzymes of the blood increase two to fourfold during pregnancy (4) indicating a higher protein metabolism which would require a corresponding increase in the activity of the thyroid. If there were not the required amount of iodine to meet that increase, then it seems reasonable to assume that a pronounced disturbance both of the fetal and maternal thyroids would result. Therefore, we contend that the great increase in the proteolytic enzymes in the blood of the pregnant woman tends to produce a condition similar to that under which fetal and maternal athyrosis is produced among domestic animals—not an abnormal condition, but still one that requires an abundant supply of iodine.

ALBUMINURIA AND TOXEMIA DURING PREGNANCY

The experiments of Hunt and Seidell (5) in which they were able to immunize animals against two to tenfold the lethal dose of different toxic substances by feeding desiccated thyroid, tend to prove that detoxication may be one of the functions of the

thyroid, though, we believe, not its sole function. During pregnancy the excessive protein metabolism tends to exhaust the fetal and maternal thyroids of their physiologically active secretions if the active constituents are not continually renewed by an abundant supply of iodine. In a more or less exhausted condition its functions as a detoxicating agent would be reduced and there would be a corresponding increase of toxic metabolites in the blood which would set up a condition of general toxemia such as may induce albuminuria. Bowen and Boothby (6) have demonstrated that, in subthyroid conditions, albuminuria can be eliminated by thyroid medication. Thus, while albuminuria and toxemia of pregnancy may be produced by other conditions, experimental evidence indicates that a lack of function of the thyroid may be a probable cause of albuminuria and toxemia during pregnancy which may be overcome by an abundant supply of iodine.

When the pregnant woman develops albuminuria some obstetricians recommend eliminating protein as much as possible from the diet. It is generally recognized, however, that the growing child has a high protein requirement, hence a treatment that tends to produce a protein starvation of the fetus does not appear to be reasonable. We contend that, unless there are secondary complications, if the activity of the thyroid is maintained by an abundant supply of iodine the metabolism of favorable proteins in reasonable amounts will proceed without distressing effects. A milk diet is sometimes recommended. It has been found that a very severe form of fetal athyrosis has been produced when pregnant sows have been given large quantities of skim milk. While a milk diet may assist in the elimination of a general toxemia, yet we wish to point out that it will probably be very disastrous to the fetus unless it be supplemented with an abundant supply of iodine.

UNECONOMIC USE OF IODINE THROUGH A PREVIOUS THYROID DISTURBANCE

In regions where fetal athyrosis is endemic the ranchmen say that gilts are likely to produce hairless pigs. For this reason it was claimed by some that sows would develop an immunity, but this claim was refuted and it was found on the contrary that sows acquired a susceptibility. That hairless pigs are so largely the product of gilts in these regions is due to the fact

that the gilts happen to be natives of the regions and are affected to a greater or less extent with a thyroid derangement.

Hart and Steenbock (2) demonstrated that when pregnant sows were given a high protein diet in close confinement, hairless pigs were produced which had the usual manifestations of the malady and the maternal thyroid was affected to a less degree. With a low protein diet they produced normal pigs. When the sows that had recently produced hairless pigs on a high protein diet were again bred and given a low protein diet, they again produced hairless pigs. The authors state that "with these mothers once there had been induced serious derangement, through the use of the first ration . . . the introduction of a lower protein level and larger amount of roughage did not act as a corrective." With sows that had produced hairless pigs three times in succession, the diet was supplemented in the fourth gestation period with a supply of iodine and they produced normal, vigorous and healthy offspring with normal thyroids. The above evidence shows that when a pregnant animal is suffering from a previous thyroid disturbance it cannot make an economic use of the available iodine, and this inability has a most disastrous effect upon the fetus when the amount of available iodine is near the border line of the amount required by the pregnant animal. This has a very vital significance, for when an individual who is affected with a thyroid disturbance becomes pregnant unless that disturbance is counterbalanced by exceptionally favorable conditions or an abundant supply of iodine, there will be a very serious arrested development of the fetus which will be subjected to a more or less severe form of fetal athyrosis and grave disturbances will be produced also in the maternal organism. McCarrison (7) after extensive observation of endemic cretinism in the Chitral and Gilgit Valleys of India has concluded that defective thyroid function in the mother is the essential factor in the production of cretinism.

From available evidence it seems incumbent to discuss here the effect upon the fetus when the parents are suffering from tetany, a disease that is generally associated with the parathyroids. Some physiologists (8) are inclined to look upon the thyroid and parathyroids as a single physiological apparatus, but for our present initial contention it is immaterial whether we consider the thyroid and parathyroid as separate and distinct

kinds of tissue with only a functional relationship or whether we look upon the parathyroids as essentially thyroidal in nature engaged in the active secretion of the same substance as the thyroid gland. McCarrison (9) reports the prevalence in India of endemic tetany, a disease of child-bearing women. There is a marked family tendency to the disease and the children of the women who suffer from tetany are frequently cretinous. The distribution is peculiarly local and appears to correspond more or less with the distribution of goitre. The seasonal prevalence of tetany, its practical limitation to the spring months, is very striking.

Dr. E. L. Hodgins of this University has called our attention to cases where the father suffered from tetany and the children have developed signs of cretinism. While the evidence to a certain extent would indicate that the thyroid disturbance of the offspring, in both the above mentioned instances, might be due to a hereditary trait, yet there is such a marked similarity in the manifestations of endemic tetany and fetal athyrosis in that both are peculiarly local and appear to correspond more or less with the distribution of goitre and both are practically confined to the spring months and the gestation period, which would lead us to believe that the influence of parental tetany was very similar to the influence of maternal athyrosis and that the arrested development of the offspring was due to an uneconomical use of the available iodine during the gestation period. This would produce an iodine starvation of the fetus resulting in fetal athyrosis. Thus we conclude that when either of the parents is suffering from a disturbance of the thyroid it appears to be imperative that the ordinary diet should be supplemented with an abundant supply of iodine throughout the gestation period and possibly also when they are suffering from a disturbance of the parathyroids.

THE SEASONAL VARIATION OF THE EFFICIENCY OF THE THYROID

Seidell and Fenger (10) found that there was a great seasonal variation in the iodine content of thyroids of sheep, cattle and hogs killed at Chicago. The iodine content was at a maximum in the summer, dropped rapidly during the winter and rose to a maximum again the following summer. Their results were obtained in such a manner that it can be concluded that their

results hold true for all the thousands of animals killed at Chicago. This fact would eliminate the factors of local environment and individual traits and also indicate that the environments of the majority of the domestic animals of this continent tend to induce a thyroid inefficiency at least during the winter months.

It has been pointed out that fetal athyrosis is practically confined to the spring litters. The results of Seidell and Fenger show that the iodine content of the thyroid of hogs is lowest from December to March, the period of the intra-uterine life of the spring litters. McCarrison (9) also reports that endemic tetany of child-bearing women, whose offspring are cretinous, is practically confied to the spring months. The corroboration of the decrease of the thyroid function during the winter months from three different, wide aspects is very striking.

What are the factors that caused this wide variation during the winter and summer months? Closer confinement and a diet consisting entirely of dried food are two outstanding winter conditions. If these may be the factors then the question arises: Will an artificial mode of life with increasing closer confinement and a decreasing amount of fresh food tend to produce a greater prevalence of a more or less acute form of fetal and maternal athyrosis? We have no direct evidence that either of the above is the controlling factor, although some investigators claim that close confinement will produce thyroid hyperplasia in certain wild animals (14). Still it appears advisable that the diet should be systematically supplemented with iodine at least under certain conditions during the first three months of the year.

THE IODINE REQUIREMENT DURING PREGNANCY

When we first made the deduction that in certain sections of this continent the available iodine was near the border line of the amount required by the pregnant animal (1) it appeared to us that one or more possible conditions varied in such a manner as to exert the controlling influence on the occurrence of the thyroid disturbance. There is a wide variation in the iodine content of farm crops, even of the same kind. Forbes and others (11) found that the iodine content of a given grain crop varied in the same field. Therefore the amount of iodine in the mother's food would appear to vary.* Fetal athyrosis is most prevalent when the gestation period is confined to the winter months when the animals are in relatively close confinement and their rations

are practically devoid of fresh fodder. Is there a variation in

*Hunziker (12) after an extensive study of goitre in Switzerland, has recently concluded that goitre is prevalent in regions where the vegetation lacks the standard proportion of iodine.

the iodine content of the fresh and dried food with regard to amount and availability? It may be pointed out that the results that have been published (11) (13) which show an entire absence or a low percentage of iodine in the common agricultural products, have been obtained practically all by analysis of the dried samples, usually in a water free condition (that is, dried for four or five hours at 100° to 110° C). Further, the desirability of fresh foods, vegetables, etc., is universally accepted. Does that metabolism which is associated with the thyroid require a greater thyroid activity with dried food than with fresh foods and therefore an increased iodine supply to maintain the increased activity? Bensley (14) claims that close confinement is the cause of thyroid hyperplasia that he observed in opossums in captivity. Does close confinement require an increase in the thyroid secretion and therefore an increase in the iodine supply? Diets that produce rapid growth appear to cause an excessive elimination of the iodine of the thyroid. May not the diets or other conditiions in certain areas produce an excessive elimination of the iodine of the thyroid and necessitate an increase in the iodine supply? Several investigators claim to have produced goitre by administration of the drinking water from certain geological formations. Whatever may be their contentions, at least it would make us suspect that the drinking water might be a possible factor in the available iodine supply, not only in actual amount, but perhaps in availability and economic use. We suspected numerous conditions that might be possible factors controlling to a certain extent the occurrence of the thyroid disturbance yet the main controlling influence might at the present time be completely masked and there was not the evidence that would lead to a clear understanding of the relation of the conditions which we did suspect, to the occurrence of the disturbance. Therefore it appeared to us to be more concise and more satisfactory to designate the controlling influences as certain unknown conditions, and, according to whether these were favorable or unfavorable, the iodine requirement of the pregnant animal would be sufficient or insufficient, and as the disturbance

could be overcome by an abundant supply of iodine that for practical purposes it was feasible to assume that the cause of the lack of function of the thyroid was a deficiency of iodine.

The human environments may not lead to such a general thyroid inefficiency as has been observed among domestic animals and while we do not wish to underestimate the importance of ascertaining all the factors that may contribute to the final condition of a deranged thyroid, yet it appears to us in the interest of public health that during those periods in the life history of the individual when the thyroid takes on an increased activity, that is during the fetal growth, pregnancy and probably puberty and menstruation, it is advisable to supplement the ordinary diets with an abundant supply of iodine in order to insure a normal development and to ward off pathological conditions. From one-half to one grain of iodine supplementing the ordinary diet approximately daily during pregnancy and menstruation and for a period of seven days each month during puberty would be sufficient to meet all the iodine requirement of the thyroid.

When iodine is adminstered as potassium iodide it is quickly detected in the urine and saliva, but in combination with fats it is retained for a relatively long period in the system, therefore it would probably be more efficient to use the iodine derivatives of the higher fatty acids. In the absence of any satisfactory organic iodine compounds any of the non-toxic iodides can be used as the source of the iodine as they would all probably be converted, in the body, into sodium iodide. Potassium iodide can be used or perhaps better still, the ferrous iodide. The beneficial results obtained when desiccated sheep thyroid was supplied to pregnant sows (1) were only very slight in comparison to those obtained when iodides were given and they appeared to be only in proportion to the iodine content. As we contend that it is essential that iodine concentration of the blood should be maintained we do not recommend desiccated animal thyroid as the source of the iodine supply because of its very low iodine content.

CONCLUSIONS

The occurrence of disorders of the teeth, nails and hair during pregnancy indicates that there is a very wide occurrence of a more or less severe form of maternal athyrosis.

The increase of the proteolytic enzymes in the blood of the pregnant woman tends to produce a condition similar to that under which fetal and maternal athyrosis is produced among domestic animals—not an abnormal condition, but still one that requires an abundant supply of iodine.

Lack of function of the thyroid is a probable cause of albuminuria and toxemia of pregnancy which may be overcome by an abundant supply of iodine.

A milk diet for the elimination of toxemia of pregnancy will probably be very disastrous to the fetus unless it be supplemented with an abundant supply of iodine.

When either of the parents is suffering from a disturbance of the thyroid it is imperative that the ordinary diet should be supplemented with an abundant supply of iodine throughout the gestation period and possibly also when they are suffering from a disturbance of the parathyroids.

To insure the normal function of the thyroid the ordinary diet should be supplemented with one-half to one grain of iodine approximately daily during pregnancy and menstruation and for a period of seven days each month during puberty, especially during the first three months of the year.

BIBLIOGRAPHY

1. Smith, G. Ennis: Fetal athyrosis. J. Biol. Chem. (N. Y.) 1917, **29,** 215.
2. Hart, E. B. and Steenbock, H.: Thyroid hyperplasia and the relation of iodine to the hairless pig problem. J. Biol. Chem. (N. Y.) 1918, **33,** 313.
3. DeLee: Principles and practices of obstetrics, 1916, 108, 112.
4. Wilson, C.: Metabolism of the pregnant woman. Bull. Johns Hopkins Hosp. (Balt.) 1916, **27,** 121.
5. Hunt, R. and Seidell, A.: Studies on thyroid. Bull. Hyg. Lab. U. S. P. H. S., 1909, 47.
6. Bowen, B. D. and Boothby, W. M.: A study of the effect of thyroid medication on the basal metabolism, renal function and nitrogen balance in chronic nephritis and in hypothyroidism. J. Urol. (Balt.) 1917, **1,** 469.
7. McCarrison, R.: Observations on endemic cretinism in the Chitral and Gilgit Valleys. Proc. Roy. Soc. London, 1908-9, II Med. 1-36.
8. Vincent, S.: Internal secretion and the ductless glands. 1912, 337-45.

9. McCarrison, R.: Endemic tetany in the Gilgit Valley. Lancet (Lond.) 1911, 1575.
10. Seidell, A. and Fenger, F.: Seasonal variations in the iodine content of the thyroid gland. J. Biol. Chem. (N. Y.) 1912-13, **13,** 517. Fenger, F.: On the seasonal variation in the iodine content of the thyroid gland. Endocrin. 1918, **2,** 98-100.
11. Forbes, E. B. and Beegle, F. M.: The iodine content of foods. Ohio Agric. Exp. Station, 1916, Bull. 299.
12. Hunziker, H.: Goiter in Switzerland. Cor. Bl. f. Schweizer Aerzte (Bern) 1918, **48,** 220; J. Am. M. Assn. (Chgo.) 1918, **70,** 1196.
13. Bohn, R. M.: The iodine content of food materials. J. Biol. Chem. (N. Y.) 1916-17, **28,** 375.
14. Bensley, R. R.: The thyroid gland of the opossum. Anat. Rec. (N. Y.) 1914, **8,** 437.

DIABETES IN INFANCY AND CHILDHOOD.

Isaac A. Abt, M.D.
Chicago.

Diabetes in children is infrequent as compared with its occurrence in adult life. Van Noorden (1) found of 3000 patients 2.8 per cent were in children under 12 years of age. In scanning the literature one is impressed by the fact that no extensive clinical studies have been made on the diabetes of infancy and childhood, and consequently no valuable contributions have emanated from this source. Many interesting clinical reports have been made, though they tend more to confirm the general knowledge of diabetes than to shed any new light on the subject. The literature of diabetes is replete with experimental studies on animals. In candor, however, it should be stated that the experimental results fail to explain fully the clinical manifestations in man.

In many instances the conditions produced in experimental studies are not duplicated in clinical diabetes. Lorand (2) says that extirpation of the thyroid suppresses glycosuria in depancreatized animals. Normally the pancreas exercises an inhibitory influence on the thyroid gland. In a depancreatized animal this influence is lost. In consequence the thyroid secretion is increased in these animals. This increase of thyroid secretion augments the quantity of adrenalin. If the thyroid is removed the secretion of adrenalin diminishes, and at the same time the hyperglycemia and glycosuria disappear. Standing out in apparent contradiction are these facts: Glycosuria has been observed in thyroidectomized animals, and in cases of myxedema diabetes has been described. How can these statements be reconciled?

From clinical studies we know that glycosuria in children occurs in a variety of conditions. Glycosuria has been observed in the newly born. Hoeniger (3) observed several times that infants delivered with forceps showed sugar in the urine for three or four days, which gradually diminished. In contradistinction to this he found children who were born after long labor remained free from sugar. This led him to believe that the trauma inflicted by the application of the forceps was suffi-

cient to induce glycosuria. There are no statistics, however, to indicate the frequency of this occurrence.

In premature babies lactose is sometimes found in the urine. Glycosuria occasionally occurs in alimentary intoxication and shows its presence in the form of lactose and galactose. Where certain foods have been administered other forms of sugar may be observed, such as saccharose, lactose and maltose. Lactosuria and galactosuria are not easily demonstrated by the ordinary copper tests. The presence of considerable ammonia in the urine interferes with the reaction (4). It is advisable to boil the urine before testing it. If the sugar content is small the copper oxide is precipitated after the test tube has been allowed to stand for a time. If one is in doubt as to the nature of reducing substance the osazone test should be applied. Saccharose does not ordinarily reduce the copper solutions. The finding of lactose in the urine is simply an indication of the increased permeability of the intestinal epithelium, permitting the sugar to pass into the blood. The presence of lactose in the urine may indicate an alimentary lactosuria without any particular illness on the part of the child. An alimentary lactosuria is sometimes observed in those children in whom a rapid change in the sugar content of the food is made.

In addition to the alimentary origin, sugar is found in the urine in organic disorders of the liver, acute infectious diseases of infancy and organic brain diseases. In syphilis, scarlet fever, enteritis, chronic enterocolitis and other infections, a transitory glycosuria has been observed. In chronic illnesses sugar may be present.

Mosenthal (5) describes renal diabetes as glycosuria, the result of increased permeability of the kidney for sugar. These are usually mild cases and have none of the grave manifestations of true diabetes. The glycosuria continues at a fairly constant level and is not markedly affected by the carbohydrate intake. The percentage of blood sugar remains normal, while the urine contains sugar. The occurrence of this condition is not frequent, and owing to the almost universal severity of diabetes in children we would doubt its frequent occurrence in early life, although Bonninger (6) reports the case of a man of 37 years who suffered from renal diabetes, whose son, age not given, suffered from the same disease. Wynhauser and Elzas (7) reported a child of 12 years who apparently suffered from renal diabetes.

Injection of potassium, calcium or normal salt solution hypodermically not infrequently produces glycosuria in babies.

True diabetes mellitus in children usually assumes a severe and progressive type of disease characterized by constant sugar production in the urine; hyperglycemia, acetone and diacetic acid are frequently present. The patient is profoundly affected, and the course of the disease, as a rule, is brief.

Concerning the age of occurrence Wageli (8), who collected 108 cases, was able to give the age of occurrence in 102, and summarizes as follows:

Age	Males	Females	Not Given	Total
Under 1 year	2	....	1	3
1-5 years	12	8	6	26
5-10 years	11	17	3	31
10-16 years	19	22	1	42
	44	47	11	102

It is to be noted that boys in the first five years are much more frequently affected. Saundby (9) collected 159 cases in 1886, with about the same results. Notwithstanding Wegeli's opinion, later tables would indicate that the sexes are equally affected. Among 6496 fatal cases of diabetes occurring in England and Wales in ten years there were but 8 patients under one year of age (10). A study of statistics would indicate that boys are more frequently affected in the first five years and that both sexes show an equal frequency from five to ten years. The peculiar circumstance has been remarked that in families in which several generations have been so struck the patients are younger the more advanced the generation. My own experience would indicate that the predilection for diabetes is not manifest in Jewish children. It would seem more than coincidence that I have seen seven to eight non-Jewish children with diabetes to one Jewish child. Heredity, undoubtedly, has an influence on the occurrence of diabetes in children, though my own observations extending over a period of years would seem to indicate that only an occasional case shows a definite hereditary influence. Notwithstanding this, Lion and Moreau (11) report 23 out of 100 cases which showed a familial occurrence of the disease. Langaker (12) reports the incidence of the dis-

ease in four children of a family of eight. These died within four years, and three of them were less than five years old at the time of death. Five years later a fifth child of the same family died at seven years. Juvenile diabetes is relatively frequent, heredity playing an important part. Lion and Moreau collected thirty instances of this type.

It has been known for some time that some relation seems to exist between trauma and transitory glycosuria. Diabetes in children has followed severe trauma not only to the head, but to the muscles and abdomen as well. In the review of 212 cases of head injuries admitted to the Boston City Hospital, Higgins and Ogden (13) found glycosuria in 20 cases. Five of them were simple scalp wounds, four deeper wounds denuding the bone, five fractures of the vault and five fractures of the base. One case was omitted.

Naunyn collected from his own clinic and the literature 50 cases of traumatic diabetes, half of which were head injuries and half injuries to other parts of the body. Two cases, which were reported by Dr. S. Strouse and myself (14) and were at the time considered mild cases, died about one year after our reporting them. One of these cases of diabetes followed a head injury and one, an abdominal. I have a case in the hospital at the present time, a child of four, whose playmate let a brick fall upon his head from a distance of four feet. This produced no severe injury, not even a scalp wound. The accident occurred seven weeks ago. One week later the patient showed marked polyuria, a voracious appetite and a loss of strength. Urinary examination on entrance showed 2.8 per cent of sugar.

Infectious diseases are recorded as an exciting cause of diabetes. Numerous authors suggest the possibility of the acute infectious diseases as an etiological factor. Von Störck (15) reports a seven-year-old girl who developed diabetes mellitus in the course of whooping cough. He suspects the child developed an infectious pancreatitis. Von Noorden conceives the possibility of a lesion of the pancreas in many of the acute infectious diseases, such as angina, influenza, measles and scarlet fever. Connective tissue changes occur in many of these diseases as well as the alimentary disturbances. This view of the cause of diabetes, no matter how attractive it may be, lacks clinical and pathological basis.

The fetus and infant are variously affected by maternal diabetes. The disease in the mother is most frequently disastrous to the fetus. Naunyn (16) says that conception does not often occur in women who are diabetic, although he reports 16 cases where women became pregnant. Premature labor with dead or macerated fetuses is a common occurrence. Naunyn reports a woman suffering from diabetes who had three successive pregnancies each of which resulted in an abortion at the 4th or 5th month. Offergeld (17) reports a series of 57 women who became pregnant. Fifty-one per cent of the children were still-born, 11 per cent died soon after birth, and 7 per cent died in infancy from hydrocephalus or diabetes, a mortality of over 66 per cent. In 25 cases in which the children died, 17 mothers died in coma. It is noteworthy to quote Naunyn, who says that there is no well-authenticated case on record where a mother gave birth to a diabetic child. This is not to say, however, that surviving children do not become diabetic in infancy.

There are very few contributions on the pathological anatomy of the pancreas in the diabetes of children. Heiberg (18) performed autopsies on four diabetic children four and a half and five years, and three and fifteen months old. He examined the pancreas particularly, and the striking pathological findings were moderate atrophy of the pancreas and diminution in the number of the islets of Langerhans. Rarely is there found degeneration of the islets. In this connection it would be well to recall the observations of Weichselbaum and Kyrle (19), who record the histological findings in the pancreas of normal infants. They found that shortly after birth the islets tend to diminish in number and do not form such large groups. The islets are not always spherical, but are inclined to be irregular in shape. They vary in size and are lined with only a few rows of cells. In diabetes round cells are sometimes found in the islets and in the immediately surrounding tissue. The observation of Heiberg coincides with the statement frequently encountered in the literature that pancreatic fibrosis does not commonly occur in the diabetes of children. In J. H. Mason Knox's case the pancreas was carefully studied. He describes small round cells in the interstitial tissue, which in some places seem to replace the acini. Connective tissue was increased. The

islets were diminished in size and number, and in one section none were seen. The capsule was thickened, and the trabeculae were visible in the connective tissue. Martins (20) found in a series of 51 cases, including four children of 3, 12, 15, and 16 years, that all showed a histological alteration of the islets of Langerhans, such as sclerosis, hyalin and hydropic degeneration. Not all of the islets, however, are involved. It seems a striking fact that severe and fatal diabetes may occur with slight or insignificant changes in the pancreas. It is also worthy of note that severe lesions of the pancreas may occur without producing glycosuria. There are some who would explain this by saying that death may occur before the symptoms of diabetes come to light or that in severe lesions of the pancreas the uninvolved portions may be sufficient for sugar metabolism. We are assured from the highest pathological authorities that severe diabetes may occur with no demonstrable lesion of the pancreas.

A careful search through the literature reveals that there are apparently no cases reported to establish a relationship between lesions of the hypophysis and diabetes in children. It appears that a true acromegaly does not occur in childhood, although a case is reported of congenital enlargement of the extremities suggesting acromegaly. This baby was brought to the clinic when it was one day old. The extremities were unusually long. The child died at two and one-half months with bronchopneumonia and a congenital heart lesion. Autopsy revealed an enlarged sella turcica and a pear-shaped hypophysis the size of a bean. Histological examination showed no definite pathology. No mention is made of glycosuria.

Lipemia occurs commonly in diabetes. Stoerk (21) reports a case of fatal diabetes in a child of ten years who had large amounts of fat in the blood and had symptoms of status lymphaticus. He quotes Klemperer, who explains lipemia in diabetics as greater cell destruction and construction, the lipemia signifying the preparation of the cell lipoids for construction of new cells.

For the sake of clearness it should be mentioned that there are those who believe that the whole glandular substance of the pancreas is primarily the cause of diabetes, but the consensus of opinion favors the view that the disease is intimately associated with the internal secretory functions residing in the

islets of Langerhans. As is admitted by every one, the islets play no part in the production of digestive secretion, but probably furnish an internal secretion regulating sugar metabolism.

The symptoms of diabetes in children are almost identical with those in adults, such as loss in weight and strength, fatigue upon slight exertion, increased appetite, polydypsia, and polyuria. Eneuresis is not an infrequent symptom. Urticaria, pruritis and eczema occur as well as furunculosis. The teeth decay early, and stomatitis is not uncommon. Edema about the face and ankles has been observed in advanced cases. Headache, backache and radiating pains in the extremities are sometimes seen. Particularly characteristic are pains in the calf muscles. The urine contains sugar, at times acetone and diacetic acid, and not infrequently albumen and casts. Morse (22) mentions an early and conspicuous symptom is irritation of the external genitalia. He also describes polyuria as the first symptom in five of seventeen patients over two years of age, although eventually it occurred in all.

Diabetes in children may begin in a mild or severe form, though it must be observed that the transition from the mild to the severe form occurs more rapidly than in adults. In some cases the disease has not been recognized until after this transition has occurred. Some children seem to improve after the sugar tolerance has been regulated and the urinary sugar kept low. They attend school and seem to progress favorably in their studies. At times they gain in weight. The temperature is inclined to be subnormal. When the glycosuria has disappeared none of the children lose their tendency toward it. Sugar returns on the slightest provocation. It reappears following psychic disturbances such as disappointment about a journey or a bad school report. Sugar also tends to return following coryza, parotitis, pharyngitis and diarrhea. In most cases the sugar tolerance can be restored, but an accumulation of insults, that is frequent recrudescences, tends gradually to reduce permanently the level of tolerance. In consequence of this fact infections of the upper respiratory tract or other infections have an ominous significance and tend to produce complications in diabetic children. In three of Kleinschmidt's (23) cases measles had a decidedly unfavorable effect. In one the disease was first discovered after the measles. In a case reported by Naunyn

varicella entailed fatal acidosis, and in Starck's case whooping cough had the same effect. In one of Kleinschmidt's cases a girl of seven suffered a severe hemorrhagic nephritis without return of the diabetes. This child had a suppurating skin infection besides the diabetes.

There are a few cases of diabetes in children reported in the literature which seem to illustrate the influence of other factors, such as glandular disturbances not pancreatic, injury to the brain and other trauma. Siegmund (24) reports that thyroid deficiency in children is often accompanied by pathological sugar hunger. Such children are able to take large quantities of sugar for long periods without glycosuria, and the sugar seems to act beneficially upon the effect of the thyroid deficiency. He states that thyroid feeding may cure this sugar hunger within two days. Alfred Gordon (25) reports two cases showing apparently a relation between the thyroid and diabetes. The patients were brothers, three and four and one-half years old. The younger gave full evidence of myxedema. His intellect was retarded, and he was quite indifferent to his surroundings. Respirations were slow and the pulse was sixty. The hair was coarse, and the skin thick and edematous. The urine had a high specific gravity and a few drops promptly reduced Fehling's solution. The child had all the symptoms of diabetes, as frequent and abundant micturition and increased thirst. The second child, four and one-half years old, had been sick for two years. There were marked symptoms of cretinism. The hair was scanty, the nails brittle, and the urine contained sugar in abundance. The findings were all more marked than in the younger brother. The children were both given thyroid gland extract. In consequence, their mental dullness, apathy and languor improved. The myxedematous condition of the skin gradually disappeared, and the color improved. The sugar diminished, and it appears conspicuous that the glycosuria cleared up more quickly than the myxedema. Eventually the sugar disappeared, and the children became more lively and playful. When the thyroid treatment was temporarily stopped the mental hebetude returned, and the sugar increased in quantity. With resumption of treatment the condition again improved promptly, and at the time of writing they were doing well even after a period of non-treatment. The family history is interesting. The

father is a neuropath, treated for obsessions, and the mother is obese and is treated for diabetes. This case report is extremely interesting and is unique. No similar cases have been observed as far as our researches reveal; and no definite deductions should be drawn as to the relation between thyroid deficiency and glycosuria. Who has not seen his quota of cretins without the slightest glycosuria? Von Noorden states it is almost impossible to set up glycosuria in animals after extirpation of the thyroid, or in human beings suffering from myxedema, as the pancreatic influence is increased by the absence of the thyroid.

Glycosuria occurs in association with neoplasms, hemorrhage and abscesses of the brain and hydrocephalus. Strauch, Hassin and Levin in a personal communication have given us a brief report of an interesting case of hydrocephalus which they will shortly publish in full. The patient was a fat girl of nine years with diabetes insipidus and such marked hydrocephalus that the cranial sutures gaped. She had long, tapering hands, although her feet were not large. There was paralysis of the eye muscles, bilateral optic neuritis and marked development of the labia majora and pubic hair. The voice was not coarse, and the blood pressure was somewhat increased. Feeding nine ounces of sugar did not produce glycosuria. Autopsy showed no involvement of the hypophysis. There was complete occlusion of the aqueduct of Sylvius, no fourth ventricle, and the lateral ventricles were as large as an ordinary brain. Jeans (26) describes a boy of three years with diabetes who had features suggesting dispituitarism, as spade-like hands, dry skin, fingers of the shape seen in acromegalics, large hands and feet and stature above normal. Knox (10) quotes several reports of brain involvement with diabetes. Hagenbach (27) in 1879 reported a case of an eight-months-old child with glycosuria, polyuria and urine of high specific gravity, whose illness lasted thirteen months. The child died with gangrene of the lungs and chronic hydrocephalus. Orloff (28) describes a case of a five-months-old child with glycosuria, hunger, thirst, polyuria and loss of weight, whose lateral ventricles were found markedly dilated on autopsy. Langstein's (29) case of a six-months-old child with repeated convulsions and urinary sugar running from 0.1 to 1.0 per cent died in a few months with internal hydrocephalus. He also had a case of a seven-day-old infant with anencephalus. This child had 0.5 to 1.0 per cent

of glucose and died nine days later. There was a complete absence of the cerebral hemispheres. Glycosuria is not infrequently associated with brain tumor. The case of Van Ordt, quoted by Falta and Meyer, is of interest in this connection. An eight-year-old girl was free from sugar when she fell ill. With aggravation of the brain tumor symptoms, 3.5 per cent of sugar was found in the urine. After restriction of the carbohydrates the urinary sugar disappeared, although it later reappeared. Autopsy revealed several miliary tubercles on the floor of the fourth ventricle and a large tumor in the region of the posterior corpora quadrigemina, pes cerebri and tegmentum pontis. The mass also involved the floor of the fourth ventricle. The pancreas, according to Van Ordt (30), was normal.

Since the work of Claude Bernard in the early part of the nineteenth century in demonstrating the piqure phenomenon, much interest has attached to the cerebral origin of diabetes mellitus. Whether the altered carbohydrate metabolism is to be explained on the basis of a carbohydrate metabolism center or by the removal of the nervous influence over the chromaffin system is far from being definitely settled. The fact remains that there are many well-authenticated cases of cerebral disease, especially lesions of the floor of the fourth ventricle, which in some unknown way produce permanent glycosuria.

As has already been pointed out, diabetes in children may be mild or severe. It is striking, however, that the younger the individual the more marked is the tendency for the disease to pass suddenly from the mild to the severe type. In my own experience such cases as I have considered mild and amenable to dietetic treatment nearly always terminated fatally in the course of several months or a few years. Nevertheless, reports of mild diabetes in children are not infrequently found in the literature, in which the authors promulgate the opinion that juvenile diabetes need by no means be considered a mortal disease. Inasmuch as the further course of those patients reported is not available, we remain in the dark as to their final outcome.

In this brief review I have attempted to outline the salient features concerning the diabetes of infancy and childhood. Such case reports were used as would illustrate the pathogenesis, symptomatology and course of the disease. Detailed reference to the extensive literature on experimental diabetes has been purposely

omitted because at the present time it is difficult to coordinate the experimental data with the clinical manifestations in adults and children.

BIBLIOGRAPHY.

1. Von Noorden: Hand. der Kinderkrank., Pfaundler u. Schlossman, 2 Auf., 1910, **11,** 117.
2. Lorand: Trans. Path. Soc. London, 1906, Pt. 13, 1-57.
3. Hoeniger: Deutsch. med. Wchnschr. (Berlin), 1911, **37,** 500.
4. Finkelstein: Sauglings Krank., Berlin, 1912, Pt. III, 318.
5. Mosenthal: Johns Hopk. Hosp. Bull. (Balto.), 1916, **27,** 133.
6. Bonninger: Deutsch. med. Wchnschr. (Berlin), 1908, **34,** 780.
7. Wynnhauser and Elzas: Abs. J. Am. M. Assn., (Chgo.) 1918, **70,** 1343.
8. Wegeli: Arch. f. Kinderheilk. (Stuttgart), 1896, **19,** 1.
9. Saundby: Lect. on diabetes, including the Bradshawe Lect., Bristol and London, 1891; quoted by Wegeli.
10. Knox: Johns Hopk. Hosp. Bull., (Balt.) 1913, **24,** 271.
11. Lion et Moreau: Arch. de Med. des Enfants, (Paris) 1909, **41,** 21.
12. Langaker: Deutsch. med. Wchnschr. (Berlin), 1911, **37,** 217.
13. Higgins and Ogden: Boston M. and S. J., 1895, **132,** 197.
14. Abt and Strouse: Am. J. Med. Sci., (Phila.) 1911, **141,** 338.
15. Von Störck: Münch. med. Wchnschr., (Münich) 1912, **11,** 24.
16. Naunyn: Nothnagel's System, 1893, 206.
17. Offergeld: Deutsch. med. Wchnschr. (Berlin), 1909, **35,** 1226.
18. Heiberg: Arch. f. Kinderheilk., (Stuttgart) 1911, **56,** 403.
19. Weischselbaum und Kyrle: Arch. f. mikr. Anat., (Bonn) 1909, Bd. 74 quoted from Heiberg.
20. Martins: Frankfort Zeitsch. f. Path., 1915, **17,** 278.
21. Stoerck: Wien. med. Wchnschr., 1911 **13,** 1298.
22. Morse: Boston M. and S. J., 1913, **168,** 533.
23. Kleinschmidt: Med. Klinik., (Berlin) 1916, **12,** 1227.
24. Siegmund: Deutsch. med. Wchnschr. (Berlin), 1910, **36,** 990.
25. Gordon: Amer. Med., (N. Y.) 1904, **7,** 229.

26. Jeans: Am. J. Dis. Child., (Chgo.) 1917, **13,** 145.
27. Hagenbach: Jahrb. f. Kinderheilk., (Leipzig) 1879, **13,** 421, from Knox.
28. Orloff: Vrach., Mar. 3, 1901; abs., Semaine Med., 1901, 192 (Knox).
29. Langstein: Verhand. d. Cong. f. innere Med., 1909, **26,** 209 (Knox).
30. Van Ordt: Deutsch. Ztschr. f. Nervenheilk, (Leipzig), 1900, **18,** 126, from Falta and Meyer, p. 554.

THE FUNCTION OF THE THYMUS GLAND*

Eduard Uhlenhuth, Ph.D.
Rockefeller Institute of Medical Research, New York

The function of the thymus gland is less well understood than that of any of the other organs usually enumerated under the terms "glands of internal secretion." The evidence in favor of the existence of a thymic hormone is extremely meagre, and for the most part is deduced from experiments, the results of which are doubtful in their bearing upon that problem. The warnings which have been raised repeatedly against a premature conception of the thymus as an endocrine gland, therefore, seem to be fully justified.

A warning has but recently been sounded by E. R. Hoskins (10). In 1918 he reviewed carefully the most important literature and was led to the conclusion that up to that time no experiments were known which deserved the credit of having proved conclusively the existence of an internal thymic secretion. Referring to the present writer's experiments (at that time incomplete) upon feeding thymus to the larvae of salamanders, he correctly stated that these could not be regarded as demonstrating an influence of the thymus gland upon growth and development. Hoskins correctly estimated the vagueness of our knowledge with regard to the function of the thymus at the time the article was written. Extensive experiments appeared, therefore, to be necessary to clear up the problem. We have now conducted such experiments on a rather large scale for several years, and have obtained positive evidence in favor of the existence of a thymic secretion. To report some of these experiments and to discuss their bearing upon the function of the thymus is the object of this article.

The animals used for these experiments were the larvae and adults of amphibians—water lizards, newts, mudpuppies, or salamanders—the latter being the correct term. These animals present certain important advantages for a study of the problem of internal secretions. First, the phenomenon of metamorphosis can be used as an indicator in quantitatively determining

*Paper read before the meeting of the Association for the study of the Internal Secretions, at Atlantic City, N. J., June 9, 1919.

the rate of development under normal and experimental conditions. The stage in question can be observed readily without killing the experimental animals or interfering otherwise with the normal progress of their development. Another most important advantage is that during the larval period amphibia lead a free life, whereas all other vertebrates spend this period of life either in the egg or in the maternal uterus. At present one of the most important requirements is to study the relation which exists between the anomalies of internal secretion in adult life and the development of the endocrine glands in embryonic life. It is during the embryonic period that the glands of internal secretion, like all other tissues, undergo the most active and profound changes, and consequently react to external factors more promptly than during adult life. In salamanders, new endocrine glands are found to develop until the time of metamorphosis, and it is not until after metamorphosis has taken place that the structures of most of the glands become stable. In these animals, the effects of all the factors suspected to have some influence upon the development of the inner secretory glands can be studied readily during the free embryonic stage, and the influence of the abnormal development of these glands upon the development and physiological condition of the organism as a whole may be observed. This advantage is not offered by any other group of vertebrate animals.

We shall report first such results as bear upon the relation of the thymus gland to development and growth. As is well known to readers of this Journal, extirpation and feeding experiments in mammals have been carried out to prove that the thymus regulates the growth of the skeleton and the teeth, the development of the sex glands, etc., but as Hoskins points out, none of these experiments has been conclusive and most of the results have been contradicted by other experimenters.

More interest was aroused by the experiments of Gudernatsch on the tadpoles of frogs and toads than by any performed on mammals. Gudernatsch (6) reported that when tadpoles are fed on thymus, the differentiation of a certain number of these animals is checked completely, while at the same time their growth is stimulated in an extraordinary way, leading to the formation of giant larvae. From these experiments which were repeated by several other investigators who got similar results,

the conclusion has been drawn that the thymus gland contains a specific hormone which inhibits development and promotes growth. Lately, however, Swingle found that thymus fed tadpoles grew and developed in a normal manner (12). It was, therefore, necessary to repeat these experiments carefully and under varying conditions.

We will report first our results bearing upon the claim that the thymus secretes a specific growth-promoting hormone. When we started the experiments with feeding calf's thymus gland to the larvae of salamanders, at first we saw no evidence of a specific growth-promoting influence (16, 17). In some thymus fed series we actually observed a greater rate of growth than in the control series, but in others a slower rate was observed. Since such differences can be easily produced by relatively small quantitative differences in dietary constituents, we concluded that in the thymus fed larvae which grew better than the controls, we were not dealing with the effects of specific *qualitative* differences, but simply with *quantitative* differences such as are presented by variations of the amount of proteins in different kinds of food.

In experiments performed at a later date, however, we could not reproduce the growth curve exhibited by our former thymus fed series; not only did these later series grow less well upon thymus feeding, but there were always a few larvae which showed a distinct and marked inhibition of growth accompanied in the later stages of the experiments by cachetic phenomena. This induced us to study carefully the records made during all our investigations and this, together with experiments (to be published elsewhere) carried out especially with the intention of clearing up this point, has brought out the fact that the researches of Gudernatsch and Swingle, together with our own earlier experiments, suffered from inexactness, in that we all overlooked the possible influence of the addition of normal food to the thymus diet. Our later experiments have revealed the fact that if larvae are fed from the beginning on thymus gland, without the addition of normal food at any time, they will show a distinct inhibition of growth; this inhibition is exhibited uniformly by every individual and even by the larvae of those species in which at first we had not observed any influence. Larvae which are fed from the beginning daily and throughout the larval period on a certain amount of normal food in addition to

the thymus diet, grow at a normal rate or even better than the controls. Larvae which are fed for only a short time (8 to 24 days) after hatching on normal food, are able to grow at a normal rate during a period of exclusively thymus feeding lasting 10 to 15 weeks.

In our first experiments, all series were kept for one to three weeks after hatching on normal diet; the records of the experiments performed by Gudernatsch and also by Swingle show that these authors have used larvae which were caught after hatching from ponds, in which they had fed on normal food, or were kept in the laboratory on a diet of algae before the beginning of the experiment, or were kept even during the experiment entirely on normal diet, the thymus being added to the water in powdered form. Obviously these experiments could not decide the problem in question. It should be mentioned here, however, that Swingle in a number of experiments in which he fed thymus to larvae hatched in the laboratory, does not mention whether or not they were fed from the beginning of the experiment on normal food, although this seems to be the case, since some of them were used a considerable time after hatching and nothing is said to indicate that they were starved animals. If, however, the larvae of these experimental series of Swingle actually were starved before beginning the thymus feeding, it is necessary to assume that the water of the locality in which the experiments were performed contains sufficient microorganisms to permit growth of the larvae. In the water used in our laboratory, which is filtered, neither the salamander larvae nor the tapoles of *Rana sylvatica* grew on an exclusively thymus diet, unless fed a normal diet during the first days following hatching. At any rate, it seems desirable that Swingle should repeat his experiments, in order to clear up this difference.

Our experiments, then, show that the thymus does not contain a specific growth-promoting substance but, on the contrary, is deficient in specific substances required for growth; if these substances are introduced into the organism even in small amounts by keeping the larvae only for a short period on normal diet, growth can proceed in a normal way. It is necessary to assume, therefore, that the substances required for growth can be stored up in the organism, or else that they are required to develop some special organs which elaborate growth-promoting

substances. Which of these two assumptions is correct available data do not determine, but judging from the facts generally known about deficiency phenomena, it is more likely that the organism can store up these substances and that growth can then go on until they are used up.

We may now discuss our results concerning the influence of thymus feeding upon development, as observed in the larvae of salamanders. It should be said at the outset that such an influence, in contradiction to Swingle's statements, can actually be demonstrated. It is not due, however, as Gudernatsch and his successors thought, to the presence in the thymus of specific development-inhibiting substances, but on the contrary to the absence from the thymus of a specific substance required for metamorphosis (23, 25); and furthermore, our experiments show that it is only the process of metamorphosis which is inhibited by thymus feeding, while other developmental phenomena can take place in a normal way (26).

We have found (23) that when normal food is added to the thymus diet, metamorphosis takes place invariably at the same time as in the controls. And, furthermore, larvae which were fed for several days after hatching on normal food, metamorphosed frequently at the normal time, even if they were later on fed exclusively on thymus gland. It is evident, therefore, that the great variability which may be observed in the results of different authors and even in the experiments of one and the same author—a variability which was observed also by the writer in his first experiments (17, 23)—is due merely to uncontrolled additions of normal food to the thymus diet. In those series in which all larvae were fed from the beginning on thymus exclusively, not one individual was able to metamorphose, as will be reported in full elsewhere.

From these experiments it is evident that the feeding of thymus gland to the amphibian larvae actually inhibits metamorphosis and that this effect is due to a deficiency of the thymus in substances which are required for metamorphosis. In a former paper (25) I assumed that the lacking substance is iodine which, as Swingle (13, 14) has shown, is necessary for metamorphosis and of which only traces are contained in the thymus gland (Baumann, 3). Of late, however, I have come to doubt the correctness of this explanation because I have

observed that the anterior lobe of the hypophysis does not inhibit metamorphosis in the same species in which metamorphosis is inhibited by thymus diet, although Baumann (3) by the same method by which he found traces of iodine in the thymus gland could not find any iodine in the hypophysis—a result which has been confirmed later on by many investigators (4, 7, 11, 27). At present we must defer discussion of what substances necessary for metamorphosis are lacking in the thymus, since our experiments on this point are not complete.

Meanwhile the reader may be referred to a report of certain experiments (25) in which it was demonstrated that besides the thyroid secretion, still another substance, the "excretor" substance, is required to induce the thyroid to excrete its hormone; metamorphosis occurs only if, in addition to the hormone, the excretor substance also is present in a definite amount.

From the foregoing statements it is evident that the belief that the thymus gland forms specific substances effecting growth and development can no longer be based upon the experiments on amphibian larvae. It seems that at present no definite proof exists that the thymus has anything to do with growth and development, although it must be admitted also that no facts are known which disprove such a function.

Moreover, a conclusion that the thymus does not produce any secretion at all by no means follows. If the larvae of certain species of salamanders (15, 16, 17, 18) are fed on thymus gland, they soon show severe convulsions of all the muscles of the body; later on the power of voluntary contractions becomes greatly impaired, and this finally leads to permanent disablement of the muscles. The appearance of these tetanic attacks resembles in every detail the convulsions which develop in mammals after removal of the parathyroids.

That this syndrome is due to the presence of a specific substance in the thymus is indicated by the following facts: Even if the larvae are fed for a considerable initial period on normal food, thymus feeding still results promptly in convulsions observable in each single individual, and which now the addition of normal food to the thymus diet does not prevent. We have replaced more than half the amount of thymus by normal diet, and yet convulsions occurred promptly in every individual. Moreover, the thymus gland is the only one among those so far

tested which produces convulsions. We have tried other nearly related tissue, such as the prescapular lymph gland and the spleen of cattle, but neither gave results. The parathyroid glands also gave negative results. It is evident, therefore, that the phenomenon in question is a specific effect of the thymus gland, due to the presence of a specific substance in the gland.

The next question is: Are these convulsions identical with those of parathyreoprival tetany, and does the thymus manufacture the toxin which is responsible for tetany? The answer is again in the affirmative (19, 22). The larvae of salamanders do not possess parathyroids, while the larvae of the closely related frogs and toads develop their parathyroids soon after hatching. If the thymus actually contains the substance causing parathyreoprival tetany, we should expect that only the larvae of salamanders would develop tetany upon thymus-feeding. This is true; the frog and toad larvae never have been observed to develop tetany. Moreover, the salamander larvae begin to develop parathyroids at the time of metamorphosis; at the same time the tetanic convulsions are checked and do not return after metamorphosis, even with continued exclusive thymus diet. So far thymus has been fed to several larvae for two years after metamorphosis without the appearance of tetany. This observation supports the assumption that the toxin contained in the thymus is antagonized by the parathyroids.

Of course the fact that calf's thymus contains a specific toxin which is capable of producing tetany in salamander larvae and which can be antagonized by the parthyroids does not possess the character of absolute proof that the mammalian thymus would excrete this substance into the blood and in the absence of the parathyroids cause tetany. There are, however, facts at hand which very conclusively show that this is exactly the case in the amphibian organism and this certainly is sufficient reason to assume that we have discovered the most important factor involved in the tetany at least of the amphibians and mammalians. In the sauropsidae in which this phenomenon has not been studied so far, the occurrence of parathyreoprival tetany is not certain.

We have observed that in the salamander larvae tetany does not occur immediately if they are fed on thymus from an early larval state (18, 22), but begins to appear in all the larvae at a

definite developmental stage. It was found that this stage corresponds with the time at which the thymus of the larvae present for the first time the aspect of functioning possessing all the cellular elements of a fully developed gland. This must be interpreted to mean that by means of thymus feeding alone not enough of the toxin can be introduced to produce tetany; but as soon as the animal's own thymus glands begin to excrete, an excess amount of the toxin is reached and tetany appears. It seems then that the amphibian thymus produces and excretes a substance of the same character as that contained in the calf's thymus, and it is most likely, therefore, that the calf's thymus not only contains, but also, like the amphibian thymus, excretes this substance. Further discussion of the role of the thymus in parathyreoprival tetany will not be offered in this article, but more data may be found in several former papers (20, 21, 24).

The relation of our findings to the function of the thymus may now be pointed out. First, it is evident that the thymus may justly be called an endocrine gland, since it excretes a specific substance, the presence of which can be demonstrated by its effects. Naturally, however, it is impossible to conceive this action as the function of the gland, since by the term function we understand an activity which in some way is required to achieve the normal physiological condition of an organism. But so far we have not been able to show that the substance which, when left in the circulation, produces tetany, exerts any other and useful effects before it is removed from the circulation by the parathyroids. However, it would be unwise to argue that because we have not found such a physiological action of the thymus, it does not exist. The lack of such knowledge should serve as a stimulus to further research.

I have pointed out in a former article (26) that during the development of the amphibian organism six groups of organs can be distinguished, the development of each of which seems to be caused by a separate chemical mechanism; while only one of them is proved to be of an endocrine nature, the same is suspected to be the case in the other five mechanisms though the exact nature of these is unknown.

Our knowledge of the role of internal secretions is only in the beginning of its development and yet it has proved to be of such importance that wherever the slightest suspicion of an inner

secretory action appears most extensive and active work should be initiated to bring to light facts upon which further studies could be based. It is my opinion that these methods alone will be able to solve the thymus problem. For this reason I think that Hoskins (10), while he was justified in claiming that the existence of a thymic hormone was not proved up to 1918, went too far when he predicted that the thymus gland would turn out to be non-endocrine. Besides, I do not think that his arguments are entirely in accord with the facts. He cites as against an inner secretory function of the thymus its lymphoid nature. The cells which make up the thymus belong to the vascular system, and their function, he says, is no more likely to be the formation of an internal secretion than is true of cells of similar appearance in other lymphoid tissues. He overlooked, however, the fact that the thymus contains beside lymphoid cells also other types whose possible function cannot well be determined merely from histological examination. Even the spleen, which also belongs to the vascular system and plays an important role in supplying the cellular elements of the blood, is believed by some to form an internal secretion (5, 8, 9).

Furthermore the extirpation experiments of Allen (1) cannot be justly claimed to prove that the thymus is a useless organ. Allen extirpated the thymus from very young frog embryos and found that they went through metamorphosis in the normal way. This is a very important result, but it does not prove by any means that the thymus is not required to maintain a normal physiological condition of an amphibian. For, first, metamorphosis, as I have shown recently, is only one part of development and that it takes place in a normal way does not prove that other developmental phenomena have also done so. Furthermore it may be possible that the thymus gland, even if it is not necessary during the larval period of amphibians, is performing a very important function during the later periods of life, or that, without the function of the thymus gland, some organs have not developed during the larval period the function of which would have become of importance after metamorphosis. Allen has not extended his experiments over a period long enough to make these points certain, but his statement that all larvae from which the thymus had been extirpated died during metamorphosis in a most conspicuous manner and in contradistinction

to the non-operated controls certainly is far more in favor of the assumption that the thymus plays an important role during the life of an amphibian than it is in favor of the opinion that the thymus is a useless organ.

How important it is to extend experiments concerning the function of endocrine organs over as long periods as possible has become evident from Allen's own experiments on the thyroid gland. Allen (2) has shown that during the larval period tadpoles from which the thyroid was extirpated were indistinguishable from normal tadpoles; it would be very wrong, however, to conclude from this that the thyroid is a useless gland. For as soon as the time comes when the larvae should metamorphose, the effect of the absence of the thyroid becomes visible in a failure of that process. This result is of very great general importance, because it shows that endocrine disturbances though they may appear late in life need not have been caused by the action of factors during this period; they may be due to factors which acted during an early embryonic period when the glands were in the state of development, their effect not becoming visible at this time because that particular function which was suppressed or disturbed by the action of these factors was not required for the maintenance of the normal condition of the organism until at a later period. Hence our opinion that the relation of inner secretory disturbances to embryonic development needs an extensive study.

It might be well to make brief mention of still another phenomenon which we have regularly observed in thymus fed salamanders. Though the experiments are not complete and an adequate explanation cannot so far be offered, it seems desirable to describe briefly the observations because more careful studies under way now will not be finished for some time.

It has been stated above that larvae which receive normal food for a short time after hatching will grow and metamorphose even if they are fed exclusively on thymus during the rest of the larval period. We were successful in obtaining quite a number of such metamorphosed thymus-fed animals. If these animals, after metamorphosis, are held at a low temperature (15°C) it is possible to keep them alive on exclusive thymus diet; such animals may grow for a considerable time just as well as worm-fed animals at the same temperature; one of them, for instance,

was growing for about two years after metamorphosis, though it had been fed on normal food only during the first 14 days after hatching. Finally, however, all of them began to exhibit signs of an edematous condition which progressed until the entire body became greatly swollen. The parotid region, the region of the thymus and of the parathyroids began to develop into large protrusions, the tongue became thick and filled up the entire mouth cavity. Everywhere the skin presented an appearance as if it were thinning out over large water-filled cavities. This condition once started progressed until the death of the animal. Weeks before the animals die they exhibit a sort of stupor and increasing debility; they frequently are found on the back and they hardly move. The heart beat also is slowed down and apparently is less vigorous than normal. During the last week or so long intervals may elapse between successive beats. The most conspicuous and extraordinary phenomenon, however, is the edema. We have observed this condition so far in the adults of two species (*Ambystoma maculatum* and *A. opacum*) the only ones fed on thymus for so long a time after metamorphosis. Recently, however, we have paid greater attention to this phenomenon and have found that edema may appear even in the larval stage of the species *A. opacum* if the larvae are fed from the beginning on thymus, but in a more moderate degree. The most peculiar form of this edema, however, was exhibited by the larvae of a third species, *A. tigrinum;* if no normal food was given before the beginning of the thymus feeding, all larvae developed, at an age of about 70 days, four balloon-like protrusions, which were filled with fluid and over which the skin was greatly thinned out. One of these accumulations of fluid was situated in the region of the heart, one on the belly and one on each side immediately back of the gills and extending from the root of the forelimb to the dorsal fin. These protrusions were of enormous size, giving the animal a shape much like a balloon. Shortly after the development of this edema all animals died.

A number of our oldest metamorphosed animals were dissected when they showed the comatous condition and while they were still alive (in order to make sure that the changes to be reported are not post-mortem changes). It was found that many parts, including the skeleton, had assumed a white and jelly-like appearance. Upon opening the abdomen large quantities of

fluid were seen. These phenomena are so conspicuous and occur so regularly that it might cause wonder that other experimenters have not observed them. Apparently this is due to the fact that no one so far as we are aware, has kept the animals long enough under observation and no one has fed them exclusively on thymus. Though, naturally, many suggestions may be ventured, we cannot yet give any real explanation of the phenomenon, since our studies concerning this point have not been completed.

SUMMARY

The thymus actually does produce an internal secretion, but one which, so far as we know at present, has only a toxic effect in that it is the factor causing the "tetania parathyreopriva." There are, however, no facts known at present to warrant the claim that the thymus gland does not produce an internal secretion which is required to maintain the normal physiological condition of the organism.

BIBLIOGRAPHY

1. Allen, B. M.: Extirpation of the thymus gland in Rana pipiens larvae. Anat. Rec. (N. Y.), 1918, **14**, 86.
2. Allen, B. M.: The results of thyroid removal in the larvae of Rana pipiens. J. Exp. Zool. (Balt.), 1918, **24**, 499.
3. Baumann, E.: Uber das Thyrojodin, Münch. Med. Wchnschr., 1896, **43**, 309.
4. Denis, W.: A note regarding the presence of iodine in the human pituitary. J. Biol. Chem. (N. Y.), 1911, **9**, 363.
5. Gachet, J. and Pachon, V.: Nouvelles expériences sur la secrétion interne de la rate, a fonction pancréatogène. Arch. de Phys. norm. et path. (Paris), 1898, 5th Series, **10**, 363.
6. Gudernatsch, I. F.: Feeding experiments on tadpoles. I. The influence of specific organs given as food on growth and differentiation. Arch. für. Entwick. d. Organ. (Leipzig), 1912, **35**, 457.
7. Halliburton, W. D., Candler, J. P. and Sikes, W. A.: The human pituitary body. Quart. Jour. Exp. Phys. (Lond.), 1909, **2**, 229.
8. Herzen, A.: Über den Einfluss der Milz auf die Bildung des Trypsins. Arch. f. d. ges. Physiol. (Bonn), 1883, **30**, 295.

9. Herzen, A.: Beiträge zur Physiologie der Verdauung. II. Älteres, Neueres und Zukünftiges über die Rolle der Milz bei der Trypsinbildung. Ibid, 1901, **84,** 115.

10. Hoskins, E. R.: Is there a thymic hormone? Endocrinology (Los Angeles), 1918, **2,** 241.

11. Simpson, S. and Hunter, A.: Relation between the thyroid and pituitary glands. Proc. Soc. Exper. Biol. and Med. (N. Y.), 1909-10, **7,** 11.

12. Swingle, W. W.: Experiments with feeding thymus glands to frog larvae. Biol. Bull. (Woods Hole), 1917, **33,** 116.

13. Swingle, W. W.: Studies on the relation of iodine to the thyroid. I. The effects of feeding iodin to normal and thyroidectomized tadpoles. J. Exp. Zool. (Balt.), 1919, **27,** 397.

14. Swingle, W. W.: Studies on the relation of iodine to the thyroid. II. Comparison of the thyroid glands of iodin-fed and normal frog larvae. Ibid, 1919, **27,** 417.

15. Uhlenhuth, E.: On the rôle of the thymus in the production of tetany. Proc. Nat. Acad. Sc. (Balt.), 1917, **3,** 517.

16. Uhlenhuth, E.: Does the thymus gland of mammals when given as food to amphibians exert any specific influence upon the organism? Proc. Soc. Exp. Biol. and Med. (N. Y.), 1917, **15,** 37.

17. Uhlenhuth, E.: Is the influence of thymus feeding upon development, metamorphosis and growth due to a specific action of that gland? J. Exp. Zool. (Balt.), 1918, **25,** 135.

18. Uhlenhuth, E.: The antagonism between thymus and parathyroid glands. J. Gen. Physiol. (N. Y.), 1918, **1,** 23.

19. Uhlenhuth, E.: Further proof of the existence of a specific tetany-producing substance in the thymus gland. Ibid, 1918, **1,** 33.

20. Uhlenhuth, E.: Parathyroids and calcium metabolism. Proc. Soc. Exp. Biol. and Med. (N. Y.), 1918, **16,** 20.

21. Uhlenhuth, E.: The influence of milk upon tetany in salamander larvae. Ibid, 1919, **16,** 51.

22. Uhlenhuth, E.: Further proof of the antagonism existing between the thymus and parathyroid. Ibid, 1919, **16,** 70.

23. Uhlenhuth, E.: Nature of the retarding influence of the thymus upon amphibian metamorphosis. J. Gen. Physiol. (N. Y.), 1919, **1,** 305.

24. Uhlenhuth, E.: Parathyroids and calcium metabolism. Ibid, 1919, **1**, 315.

25. Uhlenhuth, E.: Relation between thyroid gland, metamorphosis and growth. Ibid, 1919, **1**, 473.

26. Uhlenhuth, E.: Relation between metamorphosis and other developmental phenomena in amphibians. Ibid, 1919, **1**, 525.

27. Wells, H. G.: The presence of iodine in the human pituitary gland. J. Biol. Chem. (N. Y.), 1909-10, **7**, 259.

THE EFFECT OF SPLENECTOMY ON THE THYMUS*

F. C. Mann, M.D.

Division of Experimental Surgery and Pathology,
Mayo Clinic, Rochester, Minn.

Probably very few glands in the body have been the subject of as much barren research as the spleen and thymus, and but few positive statements can be made with regard to the function of either of the glands. They do not appear to be necessary for life and their loss produces little demonstrable change which may be the reason we know so little about their functions.

Both the glands are lymphoid in character; this is believed from clinical and experimental standpoints to establish a definite relationship between them. A few deaths have been reported which seemed to have some connection with a large thymus and atrophic spleen (Avellis). The investigators of the thymus have been more insistent on a relationship between the two organs than the investigators of the spleen. Friedleben seems to have been the first to hint that such a relationship exists. In Basch's experiments the removal of the spleen in a thymectomized animal did not produce any effect. Klose claimed that the spleen is the principal compensatory organ of the thymus. He found that the spleen, at first much enlarged after thymectomy, later seemed to undergo functional atrophy; its removal in some of the thymectomized animals produced death. Klose and Vogt assumed that the adult spleen undertakes the function of the thymus when the latter regresses and suggested that the thymus compensates for the spleen when the latter is removed. Soli found the weight of the spleen in chickens and rabbits unaffected by thymectomy. Lucien and Parisot also found the weight of the spleen unchanged after thymectomy, but in certain cases they observed an increase in the number and the size of follicles. Perrier found an increase in the lymphatic tissue of the spleen and the presence of very large germinating centers in the follicles after thymectomy. Magnini claimed there is a hypertrophy of the spleen in both young and adult rats after thymectomy. Matti found primary hyperplasia followed by atrophy of the spleen after thymectomy; he also reported hyperplasia of

*Submitted for publication July 9, 1919.

the thymus following splenectomy in the dog. Bayer stated that there is a mutual compensation between the spleen and the thymus. If the spleen is removed the function of the thymus becomes more efficient; if the thymus is removed the spleen becomes more active. Pappenheimer, in his careful study of the effect of early extirpation of the thymus in rats, was not able to detect any alteration in the spleen. Many other studies have been made on the effect of thymectomy or splenectomy in various species of animals such as guinea pigs (12), rats (17), dogs (16, 8, 13), but little or no mention has been made of the thymus. This brief review of the pertinent literature shows that the so-called pluriglandular theory has been applied to the spleen and thymus with the usual lack of discrimination and substantial data.

In my series of experiments on animals from which the spleen had been removed for various purposes the thymus was observed regularly. As nothing definite was determined, although some suggestive material was obtained, a special series of experiments was performed for the specific purpose of determining whether or not splenectomy produces any effect on the thymus. Observations on the thymus after removal of the spleen have been made on both adult and very young animals of several species. Since the thymus regresses and almost disappears early in life it would seem that should any effect of removal of the spleen be demonstrable, the splenectomy would have to be performed on very young animals. The spleen was therefore removed just as early in life as the animals were considered able to withstand the operation successfully. One or more members of the same litter or of the same age were kept as controls. In some instances one of a litter was killed and the thymus removed and weighed at the time of operation and beginning observations of the animal used in the experiment.

All operations were performed under anesthesia, with sterile technic. The young animals were placed in an incubator immediately after operation because their temperature controlling mechanisms were not very stable. Many of the animals died from intercurrent disease, but enough data were secured to justify certain conclusions. At necropsy a careful examination for thymic tissue was made and when any was found it was fixed in Zenker's solution without acetic acid and weighed

twenty-four hours after fixation. Since the tissue removed frequently consisted mainly or wholly of fat it was necessary to make several sections of the specimen in order to estimate the amount of thymic tissue present. The position of the thymus or thymic tissue varies with different species of animals. In instances in which no thymic tissue could be found grossly in the thorax and the neck, a histologic search was seldom made because small amounts of such tissue may usually be found microscopically in the normal adult animals.

Observations were made on 25 adult dogs from which the spleens had been removed at different periods varying from a few weeks to two years. The thymus of these animals did not differ from that of normal dogs. In a very few animals of the series a small amount of thymic tissue could be found, but in most instances it could not be noted grossly. The same variability in the amount of thymic tissue may be observed in normal adult dogs.

The spleens were removed from 16 puppies ranging in age from three to six weeks. Thirteen puppies belonging to the same litters were kept as controls. As is often the case, distemper killed most of the puppies within a short time after observations were begun, but a few of them lived several weeks and one lived eleven months after splenectomy. No difference in the thymic tissue of the splenectomized puppies and of their controls was noted, although a great variability in the amount was found in the different animals, even of the same litter. One puppy would have a large thymus, while another of the same litter would have only a trace of thymic tissue. No grossly discernible thymic tissue was found at necropsy in the splenectomized puppy that lived for eleven months after operation.

A few kittens were used in the investigation; no conclusions could be drawn. The kittens were found to have practically no thymus by the time they were old enough to be operated on safely.

Observations were made on 75 adult rabbits from which the spleen had been removed at different periods varying from a few days to two years. Very rarely was any thymic tissue found and when found the amount was small. With one exception the splenectomized rabbits did not have more thymic tissue than the controls.

Spleens were removed from 21 young rabbits ranging in age from five to nine weeks. Twelve rabbits belonging to the same litters were kept as controls. Great variation in the size of the thymus was found even in the animals of the same litters. Splenectomy did not, however, cause an increase in the thymus, nor apparently any earlier regression of the organ.

In observations made on a large series of normal adult goats only a small amount, if any, thymic tissue could be recognized grossly. However, at necropsy of a very old goat (Goat 50), from which the spleen had been removed in another experiment, a large thymus was found. This seems to indicate that the lack of the spleen might be a cause of the enlargement of the thymus, although the experiment was complicated by other factors, such as the administration of cholesterin, and the X-ray. Accordingly several careful experiments were carried out on young goats. Normal data were obtained from goats of various ages that had been used in other experiments, and it was found that the size of the thymus varied greatly.

The spleens were removed from eight kids slightly less than a month old. Four other kids of the same age were kept as controls. The thymuses of a few other kids that died shortly after birth, were studied for controls. At birth and during the first few weeks of life the thymus is usually quite large, but even at this age individual variation is marked. Most of the kids withstood splenectomy well, then died or were killed at various periods of time after operation. A careful review of the results does not show any difference in the thymus of the splenectomized animals and that of the controls (Table 1 and protocols of goats).

An attempt was made by microscopic study not only to estimate the amount of thymic tissue in relation to the fat, but also to gauge the possible activity of the gland from its general appearance, number of Hassall's corpuscles, etc. Decided variations were found, but there was no evidence that splenectomy produced any specific change.

Luckhardt has made some suggestive observations with regard to splenectomy in very young rabbits and dogs. (8) Tachigara and Takagi apparently did not note much difference between the effects of splenectomy in the puppy and in the adult dog. Our results show that some animals from which the spleen

TABLE I.

SALIENT DATA OF THE MOST IMPORTANT EXPERIMENTS PERFORMED ON GOATS.

Goat	Sex	Age at Time of Operation, Days	Weight at Time of Operation, kg.	Operation	Time From Operation to Necropsy, days	Weight at Time of Death, kg.	Weight of Thymus, gm.	Estimated Amount of Thymic Tissue in Mass Weighed
77	M	25	5.0	Splenectomy	318	15.5	0.9	20 per cent
78	M	25	5.2	Splenectomy	327	15.9	1.0	50 per cent
79	F	25	5.6	Splenectomy	490	16.5	0.9	50 per cent
80	F	25	5.1	Control	483	23	0.85	35 per cent
81	M	25	4.9	Splenectomy	174	24	1.6	90 per cent
82	F	25	5.4	Control	490	14.5	1.52	75 per cent
83	M	28	4.9	Splenectomy	9	3.15	3.3	85 per cent
84	M	28	4.8	Control	18	4.0	3.9	85 per cent

has been removed quite early in life develop in the same fashion as the unoperated controls; furthermore, no definite specific change in the development due to the loss of the spleen was observed in any of the animals. Most of the splenectomized animals died before the controls died, however, and under the same conditions that the controls were developing normally. While removal of the spleen in the young did not produce any noteworthy change in development, it seemed to make the animal less able to withstand the stress of life. In order to obviate the possibility of false conclusions owing to this individual variability in the thymus it might be of value to perform the experiments on rats as that species has been carefully standardized. It should also be remembered that since rarely some effect of splenectomy has been noted on other tissues, such as the bone marrow and lymph nodes, it is possible that a larger series of experiments might have contained one or more that were positive.

PROTOCOLS

Goat 50. A very old female angora goat weighing 98.8 kg. was admitted to the laboratory Sept. 15, 1916, and was used by Dr. Luden in making cholesterol observations. January 5, 1917 the spleen was removed successfully. Complete healing followed slight infection of the abdominal wound. Beginning February 26 the animal was given cholesterin and a few X-ray treatments. She gave birth to a kid April 17 and died June 17, at which time she weighed 36 kg. At necropsy a large thymus (4 gm.) was found. Histologically the thymic tissue appeared to be very active; approximately 90 per cent of the tissue weighed was thymic.

Goat 79. A female angora goat, one month old, weighing 5.6 kg., was splenectomized March 22, 1918. The weight of the spleen was 20 gm. The animal recovered from the operation and remained in excellent condition. It was allowed to run with its mother on pasture, where it seemed to grow and develop normally. At the end of four months the animal did not differ noticeably from the controls. It weighed 18.2 kg. at this time. February, 1919, when the animal was returned to the laboratory, it weighed 22 kg. A series of blood counts, hemoglobin estimations, etc., was made; all counts fell within the normal limits. The animal lost some weight in the laboratory; on May 25 it weighed 21.3 kg., but it remained in good condition until June, by which time its weight had decreased to 16.5 kg. This loss of weight was attributed to the loss of its hair, which had been sheared, and to the confinement in the laboratory, since the control also lost weight under the same circumstances. The animal was killed by bleeding under ether, and necropsy (300) was performed immediately after death; except for

the emaciation the animal was normal. The operative wound was healed perfectly; there were no adhesions. A small amount of thymic tissue was found. This was fixed in Zenker's solution without acetic acid and twenty-four hours after fixation it weighed 900 mg. Microscopic examination showed that about 50 per cent of the weighed tissue was thymic. There were many Hassall's corpuscles; the hemolymph nodes were undoubtedly greatly increased in this animal.

Goat 82. A female angora goat one month old was splenectomized March 22, 1918. The kid was allowed to run with its mother on pasture, where it developed normally. August 1 its weight was 20 kg.; February, 1919, it was returned to the laboratory weighing 24 kg. A series of blood counts, hemoglobin estimations, etc., was made; all counts were normal. The animal lost slightly in weight in the laboratory, but remained in good condition until June 25, when its weight had decreased to 14.5 kg. One month before the animal had weighed 29.5 kg. The loss of weight was attributed to the loss of hair which had been sheared, and to the confinement in the laboratory. The animal was killed by bleeding under ether. Necropsy (301) was performed immediately. The animal was emaciated, but perfectly normal. A small amount of thymic tissue was found and fixed in Zenker's solution without acetic acid; twenty-four hours after fixation it weighed 1520 mg. Microscopic examination showed about 75 per cent of the weighed tissue to be thymic. There were but few Hassall's corpuscles. There were practically no hemolymph nodes; a few, measuring 2 mm. in diameter, were with difficulty found for microscopic study.

BIBLIOGRAPHY

1. Avellis (G.) Epikrise eines Falles von nicht ganz plötzlichem Thymustod, verursacht durch (vircariirende) Thymus-Vergrösserung bei rudimentär kleiner Milzanlage. Arch. f. Laryngol. u. Rhinol. (Berlin), 1898, **8**, 159-167.
2. Basch, (K.) Über Ausschaltung der Thymusdrüse. Wien. klin. Wchnschr., 1903, **16**, 893-896.
3. Bayer (R.) Weitere Untersuchungen über die Funktionen der Milz, vornehmlich ihre Rolle im Eisenstoffwechsel, mit besonderer Berücksichtigung des Morbus Banti. Mitt. a.d. Grenzgeb. d. Med. u. Chir. (Jena), 1914, **27**, 311-339.
4. Friedleben. Quoted by Matti.
5. Klose, (H.) Ueber Thymusexstirpation und ihre Folgen. Arch. f. klin. Chir. (Berlin), 1910, **92**, 1125-1141.
6. Klose (H.) and Vogt (H.) Klinik und Biologie der Thymusdrüse. Mit besonderer Berücksichtigung ihrer Beziehungen zu Knochen- und Nervensystem. Beitr. z. klin. Chir. (Tübing), 1910, **69**, 1-200.

7. Lucien (M.) and Parisot (J.) Contribution a l'étude des fonctions du thymus. Arch. de méd. exper. et d'anat. path. (Paris), 1910, **22,** 98-137.
8. Luckhardt. Data presented before the American Physiological Society, December, 1917.
9. Magnini (M.) Le funzioni del timo ed i rapporti fra timo e milza. Arch. di fisiol. (Firenze), 1912-1913, **11,** 333-354.
10. Matti (H.) Untersuchungen über die Wirkung experimenteller Ausschaltung der Thymusdrüse. Mitt. a.d. Grenzgeb. d. Med. u. Chir. (Jena), 1912, **24,** 665-821.
11. Pappenheimer (A. M.) The effects of early extirpation of the thymus in albino rats. Jour. Exper. Med. (N. Y.), 1914, **19,** 318-338.
12. Park (E. A.) Extirpation of the thymus in the guinea pig. Jour. Exper. Med. (N. Y.), 1917, **25,** 129-152.
13. Pearce (R. M.), Krumbhaar (E. B.) and Frazier (C. H.) The spleen and anemia. Experimental and clinical studies. Philadelphia, Lippincott, 1918, 419 pp.
14. Perrier (C.) Modifications histologiques de l'hypophyse et de la rate consécutives á la thymectomie. Rev. med. de la Suisse Rom. (Genéve), 1910, **30,** 839-854.
15. Soli (U.) Comment se comportent les testicules chez les animaux privés de thymus. Arch. ital. di biol., 1907, **47,** 115-122. Contribution á la connaissance de la fonction du thymus chez le poulet et chez quelques mammiféres. Arch. ital. de biol. (Rome), 1909-1910, **52,** 353-370.
16. Tachigara (S.) and Takagi (T.) Über die Erythroblastose und die Blutveränderung nach der Milzexstirpation beim neugeborenen Hunde. Mitt. a. d. med. Fak. d. k. Univ. Tokyo, 1917, **17,** 563-595.
17. Wolferth (C. C.) Blood changes in albino rats following removal of the spleen. Arch. Int. Med. (Chgo.), 1917, **19,** 105-116.

THE FUNCTIONS OF THE INTERNAL SECRETION OF THE PLACENTA

Frederick S. Hammett,

Pennsylvania Hospital, Department for Mental and Nervous Diseases, Philadelphia, Pennsylvania

From 1884 on, when Johannes Müller (1), designated the placenta as one of the secretory glands, the amount of investigation devoted to attempts at determining the functions of the elaboration has been so cumulatively stupendous in its complexity that any presentation in detail of the literature would be out of the question save in a monograph devoted to the subject.

A retrospective analysis of the work undertaken reveals, however, four fairly distinct nuclei of attention, although it must be said that the investigations from the point of view of quantity bear but little relation to the validity of the findings in the respective fields of endeavor.

Apparently the most potent nucleus of attention was that around which has gathered the controversy regarding the role played by the placenta in the development of eclampsia. With the discovery by Schmorl (2) of the presence of emboli of placental cells in the blood vessels of eclamptics there originated the idea that this not infrequent accompaniment of pregnancy was due to the placenta. The gradual accumulation of experimental results gave rise to three fundamentally different conceptions. The first of these hypotheses attributed as the cause of eclampsia the giving off from the placenta of protein material foreign to the host, and the inadequate elaboration of an antibody "syncytiolysin"; around this idea of Veit (3) revolved the work of Ascoli (4), Weichardt (5), Shenk (6, 7), Liepmann (8, 9), and others, but the entire series of experiments and conclusions therefrom was repudiated by the work of Licthenstein (10, 11, 12), Dryfuss (13), Freund (14), and Mathes (15, 16). The second idea supported by Hofbauer (17, 18), Dienst (19), Dryfuss (20), and others, attributed the etiology of eclampsia to an escape of the placental enzymes into the maternal blood stream in excess, with subsequent development of toxic products. Not as opposed to the latter hypothesis as a contributing cause, but as considering it inadequate, Lichtenstein (21), proposed the idea that the origin

of eclampsia does not lie in the production by the placenta of toxic material *per se*, but in the possibility that through a perversion or diminution, or both, of placental function the metabolic by-products are allowed to escape in quantity into the maternal system and there being present in addition to those produced by the maternal organism as the result of its own metabolism, put such additional burden upon the excretory and detoxicating organs that they can not adequately deal with it, and toxemia results. In a monograph by Hofbauer (22), are collected the references and evidence of the metabolic activities of the placenta up to 1905, which clearly indicate that the placenta plays a significant part in the preparatory metabolism for both mother and foetus. Quite recently it has been shown that the placenta can readily form urea (23), and it is well known that the formation of urea by the organism is the method by which the body prepares the greater part of its nitrogenous by-products for excretion. Moreover, further evidence has been adduced in the fact that placentas from toxic pregnancies contain a much higher urea content than do those from normal pregnancies (24), and it is evident from the work of Marshall and Davis (25), that due to the ready diffusibility of urea this substance must accordingly be present in higher concentration throughout the tissues of eclamptics than in the tissues of those in normal pregnancy. In addition, histological studies by Dr. J. L. Bremer, which have not yet been published, strongly indicate that in the placentas of eclamptics there is a markedly increased transformation of the syncytium into a squamous type of cell thinly overlying the foetal placental blood vessels which points to the probability of an increased permeability in these cases. *It accordingly appears probable that the cause of eclampsia does not lie in any inherent production of a secretion by the placenta, but rather that this disorder comes from a decrease, or perversion, or both, of the intermediary metabolic function of the placenta accompanied by an increased permeability of the endothelium covering the villi projecting into the maternal sinuses; the combined effect of this increased permeability and decreased detoxicating activity being a flooding of the maternal organism with the incompletely hydrolysed by-products of the foetal metabolism, putting such extra burden upon the liver and kidneys of the mother that these tis-*

sues break down, with the characteristic manifestations of an acute toxemia.

In the search for the specific source of the substance causing hyperplasia of the mammary gland during pregnancy it was but natural that the placenta received much experimental attention, since this tissue occurs concomitantly with the marked development of the mammae immediately preparatory to the taking up of the function of supplying nourishment for the infant. The investigations along this line consisted mainly in administering placental extracts prepared in a variety of ways, either subcutaneously or intraperitoneally. The apparently conflicting results have given rise to no little controversy, but although Fellner (26), Halban (27), and Cohn (28), seem to have obtained a type of response indicating that the placenta does in part, at least, contribute stimulus to mammary hyperplasia in virgins yet the mass of experimental evidence produced by Biedl (29), Biedl and Königstein (30), Basch (31), Frank (32), Frank and Unger (33), Foá (34), Lane-Claypon and Starling (35), and others seems to disprove the idea in a satisfactory manner, and more particularly since the work of the latter investigators, which has also been confirmed by Foá (36), and Biedl (37), gives conclusive evidence of the stimulating effect of extracts of tissues of the foetus upon mammary hyperplasia. In an experiment carried on at the Boston Lying-in Hospital during the winter of 1917-1918, it was impossible to detect by bedside observation any increased growth of mammary tissue when desiccated placenta was fed postpartum to lactating women, as compared with a series of patients not receiving the placental material (38). It is, of course, obvious that we were here dealing with a condition much different from that occurring during pregnancy and that the negative results may mean little or nothing as evidence towards the part played by the placenta in pregnancy hyperplasia, nevertheless, the validity of the interpretation is on a par, until disproved, with that given from the work on virgin animals. *From the evidence at hand it is reasonably certain that the placenta has but little if any direct influence upon the mammary hyperplasia of pregnancy, the source of the stimulus of this development lying in part in the foetus.*

The mammary hyperplasia of pregnancy is but the preparation of the glands for the secretory function of producing milk,

and the question as to the source of the stimulus initiating and maintaining this function throughout the period of lactation has been a subject of much study. A very comprehensive bibliography on milk secretion compiled by Rothschild (39), contains references to most of the investigations up to 1904. The studies of Goltz (40), Ribbert (41), and Pfister (42), have shown quite conclusively that direct nerve stimulation is a relatively unimportant factor. This demonstration of the dependence of the secretory function of the mammae upon the elaboration of a hormone led Halban (43), to a series of experiments in which he successively eliminated the ovaries, uterus, and foetus as the cause, and to the conclusion that the placenta during pregnancy gives off a substance acting as a chalone to milk secretion which, on its removal at term, allows the secretory function to be taken up. This was supported by Hildebrandt (44). Basch (45), Lederer and Pribram (46), and Aschner and Grigoriu (47), Bouchacourt (48), and Niklas (49), claim to have obtained an increased milk secretion on administration of placental extracts and the latter considers that at delivery there is an overflowing of placental hormones into the maternal blood which, after a certain period of incubation, brings about the initiation of the secretory activity of the milk producing cells. Yet this idea fails to explain the continued secretion of milk during the period of lactation. On the other hand, Mandl (50), Lane-Claypon and Starling (51), Mackenzie (52), Gaines (53), Fieux (54), and others, have been unable to find any valid evidence of increased milk secretion due to the placenta. More recently Van Hoosen (55), and Cornell (56), have concluded from feeding experiments with desiccated placenta that this tissue acts as a galactagogue, Van Hoosen (57) definitely claiming to have obtained an increased milk secretion and Cornell (58) basing his conclusions on an increased growth of the breast-fed infants. However that may be, in a short series of experiments carried on at the Los Angeles County Hospital and reported in two publications, one by McNeile (59), and one by McNeile and the author (60), and in a longer series of experiments in which over three hundred women were fed 10 grains of desiccated placenta three times a day (61), it was impossible to detect any increased secretion of milk as the result of the ingestion of this material when compared with the secretory activity of the mammae of patients not receiving the material. No pub-

lished reports having appeared giving results of consecutive analyses of human milk produced under the influence of the ingestion of desiccated placenta, McNeile and I (62), carried on a research designed to demonstrate whether or not the maternal ingestion of desiccated placenta would alter in any way the chemical composition of the milk produced when compared with that from lactating women under identical conditions of diet and environment but not receiving the desiccated placenta (63). As a result of our investigations it was found that *although there was no apparent stimulation leading to an increased supply of milk there was exerted upon the secretory function of the mammary gland an influence tending to raise the level of protein and lactose production with a decrease in fat elaboration.*

This alteration in composition, however, was not attributable to the food value of the ingested placental material since the amount was hardly a gram a day. *It is therefore possible to conclude that the evidence at present available does not permit us to assign a galactogogic activity to the placenta, and that its only influence upon milk secretion is slightly to raise the level of protein and lactose production while lowering that of fat.*

The fourth and most recent nucleus of attention in the search for the evidence of the placental production of an internal secretion has been the question of the influence of the placenta on growth. A number of direct feeding experiments have been carried on, but they give no evidence of a specific growth promoting substance in the placenta since the increased growth may well have been due to the addition to the diet of a supply of amino-acids in sufficient relative quantity to cause the observed effect. Van Hoosen (64), however, noticed increased growth of breast-fed infants when the mothers were fed desiccated placenta, as compared with infants subsisting upon milk from mothers not receiving the placental material. However, the general plan and scope of the work did not allow the drawing of any valid conclusions, although taken together with the note by Hammett and McNeile (65), and the work on the galactagogic action of the placenta by Cornell (66), pointed to the possibility that the feeding of desiccated placenta to nursing mothers had some effect on the growth of the breast-fed infants. Cornell found that 87 per cent of those infants receiving milk from mothers ingesting desiccated placenta had regained their birth weight by the 4th or 5th day, as com-

pared with a 67 per cent regain for the infants ingesting milk from mothers not receiving the placental material. He wrongly attributes this favorable effect to a galactogogic activity of the placenta, as it has been shown above that the ingestion of desiccated placenta fails to increase the secretion of milk, and as it will be later shown, the caloric increase in the milk, due to the action of the placenta ingested upon the secretory functions of the mammae is insufficient to account for the gain in weight ob served.

During the winter of 1917-1918 I carried on a series of experiments at the Boston Lying-in Hospital with the view to determining whether or not the maternal ingestion of desiccated placenta, as prepared according to the earlier report (67), would cause an appreciable difference in the rate of growth of the breast-fed infants when compared with that observed in normal breast-fed infants. The data for the normal growth curves were obtained from the weights of 537 infants born at the Boston Lying-in Hospital, taken on the 1st, 3rd, 5th, 7th, 9th, 11th and 13th days after delivery. Figures were taken only from those infants whose sole nourishment was derived from the maternal breast (68). Having thus obtained a standard based on the methods of weighing, care, and diet in use at that hospital, and which was necessary for any valid investigation of this nature, every patient was given 10 grains of the desiccated placenta in a capsule three times a day for two weeks, until a sufficient number of observations had been made to give valid indications. The conditions as to diet, weighing and so forth were the same as obtained with the cases where no placenta was fed. The growth curves of 177 infants were obtained from the weights of the infants on the 1st, 3rd, 5th, 7th, 9th, 11th and 13th days after delivery. As a result of this investigation it was determined that the effect of the ingestion of desiccated placenta by the mothers on the growth of the breast-fed infants is a lessened post-natal decline in weight, a quickened recovery from the preliminary loss, an increase of over 60 per cent in the rate of growth by the 13th day and an increase in the growth capacity when compared with similar figures obtained from infants receiving nourishment from others not ingesting the desiccated placenta. In view of these facts, and having, in addition, evidence that the increased food value of the milk produced during the administration of the dried placenta cannot

of itself compensate for the increased growth, and, moreover, since but 30 grains or less than a gram of the dried material was fed each day, a quantity so small as to be negligible as matter from which new tissue can be built, *it is evident that there is produced in the placenta some substance capable of acting as a stimulus to growth, when ingested by the mother and passed on to the infant in the lacteal secretion, and it is not illogical to suppose that the placenta in utero produces a substance acting as a stimulus to the foetal growth.*

SUMMARY

The evidence now available concerning the functions of the internal secretion of the placenta eliminates the probability of the participation of such a substance in the production of eclampsia, in the hyperplasia of the mammary glands during pregnancy, or in the secretory function of the mammary glands from a quantity point of view. The feeding of desiccated placenta to nursing mothers does affect slightly the chemical composition of the milk produced, but not significantly. It is, however, certain that there is in the placenta a substance which, when fed to nursing mothers, is passed on in the milk to the infants and acts as a stimulus to growth and it is this and this alone that permits the designation of the placenta as an endocrine gland.

BIBLIOGRAPHY

1. Müller, Johannes, Lehrbuch der Physiologie. I. Kloblenz, 1844.
2. Schmorl, G., Pathologisches-anatomisches Untersuchungen über puerperale Eklampsie. Leipzig, 1893.
3. Veit, D., Verschleppung der Chorionzotten. Weisbaden, 1905.
4. Ascoli, G., Vorlesungen uber Urämie. Jena, 1903.
5. Weichardt, W., Zur placentären Theorie der Eklampsieätiologie. Arch. f. Gynäk. (Berlin), 1909, **87,** 655.
6. Shenk, F., Ueber besonderheiten der Giftwirkung des menschlichen Placentasaftes beim Kanninchen. Centbl. f. Gynäk. (Leipzig), 1909, **33,** 1500.
7. Shenk, F., Schutzeffekte normaler Sera gegen die Wirkung menschlichen Placentasaftes beim Kanninchen. Centbl. f. Gynäk. (Leipzig), 1909, **33,** 1353.
8. Liepmann, A., Zur Technik und Kritik der Placentaforschung. Centbl. f. Gynäk. (Leipzig), 1909, **33,** 379.
9. Leipmann, A., Zur Technik und Kritik der Placentaforschung. Centbl. f. Gynäk. (Leipzig), 1909, **33,** 138.

10. Lichtenstein, W., Kritische und experimentelle Studien zur Toxicologie der Placenta, zugleich Beitrag gegen die placentäre Theorie der Eklampsieätiologie. Arch. f. Gynäk. (Berlin), 1908, **86,** 434. (Literature).
11. Lichtenstein, W., Gegen die placentäre Theorie der Eklampsieätiologie. Centbl. f. Gynäk. (Leipzig), 1909, **33,** 265.
12. Lichtenstein, W., Im Kampfe gegen die placentäre Theorie der Eklampsieätiologie. Centbl. f. Gynäk. (Leipzig), 1909, **33,** 1313.
13. Dryfuss, J., Chemische Untersuchungen uber die Ätiologie der Eklampsie. Biochem. Centbl. (Berlin), 1909, **7,** 492.
14. Freund, R., Zur plazentären Eklampsieätiologie. Berlin klin. Wochenschr. 1909, **15,** 682.
15. Mathés, P., Zur Theorie der Intoxikation der Mutter durch die Frucht. Centbl. f. Gynäk. (Leipzig), 1909, **32,** 1548.
16. Mathés, P., Zur Toxicologie der Placenta. Centbl. f. Gynäk. (Leipzig), 1909, **32,** 1548.
17. Hofbauer, J., Für die placentäre Theorie der Eklampsieätiologie. Zentbl., f. Gynäk. (Leipzig), 1908, **32,** 1469.
18. Hofbauer, J., Beiträge zur Aetiologie und zur Klinik der Graviditätstoxicosen. Ztschr. f. Geburtsch. u. Gynäk. (Stuttgart), 1907, **61,** 200.
19. Dienst, A., Die Pathogenese der Eklampsie und ihre Beziehung zur normalen Schwangerschaft, zum Hydrops, und zur Schwangerschaftsniere. Arch. f. Gynäk. (Berlin), 1908, **86,** 314.
20. Dryfuss, J., loc. cit. 13.
21. Lichtenstein; loc. cit. 10.
22. Hofbauer, J., Grundzüge einer Biologie der menschlichen Plazenta mit besonderer Berüchtsichtigung der Fragen der fötalen Ernahrung. Wein. Leipzig; Wilhelm Braumüller, 1905.
23. Hammett, F. S., Urea formation by the placenta. Jour. Biol. Chem. (N. Y.), 1919, **37,** 105.
24. Hammett, F. S., The Urea content of placentas from normal and toxemic pregnancies. Jour. Biol. Chem. (N. Y.), 1918, **34,** 515.
25. Marshall, E. K., Jr., and Davis, D. M., Urea; Its distribution in and elimination from the body. Jour. Biol. Chem. (N. Y.), 1914, **18,** 53.
26. Fellner, O. O., Experimentelle Untersuchungen über die Wirkung von Gewebsextracten aus der Plazenta und den weiblichen Sexualorganen auf das Genitale. Arch. f. Gynäk. (Berlin), 1913, **100,** 641.

27. Halban, J., Die innere Secretion von Ovarium und Placenta und ihre Bedeutung für die function der Milchdrüse. Arch. f. Gynäk. (Berlin), 1905, **75**, 353.
28. Cohn, F., Die innere Secretorischen Beziehungen zwischen Mamma und Ovarium. Monatsch. f. Geburtsch. u. Gynäk. (Berlin), 1913, **37**, 93.
29. Biedl, A., Internal Secretory Organs. Page 374, New York, 1913.
30. Biedl, A., and Königstein, R., Untersuchungen über das Brustdrüsenhormon der Graviditat. Ztschr. f. exper. Pathol, u. Therap. (Berlin), 1910, **8**, 358.
31. Basch, K., Über experimentelle auslösung der Milchabsonderung. Monatsch. f. Kinderheilkunde (Leipzig), 1909, **9**, 8.
32. Frank, R. T., Zur Frage der experimentellen Milchauslösung. Arch. f. Gynäk. (Berlin), 1912, **97**, 183.
33. Frank, R. T., and Unger, A., An experimental study of the causes which produce the growth of the mammary gland. Arch. Int. Med (Chgo.), 1912, **7**, 812.
34. Foá, C., Sui fattori che determinato la funzione della ghiandola mammaria. Archiv. fisiol. (Firenze), 1907, **5**, 520.
35. Lane-Claypon, Janet E. and Starling, E. H., An experimental enquiry into the factors which determine the growth and activity of the mammary glands. Proc. Roy. Soc. (Lond.), Series B, 1906, **77**, 505.
36. Foá; loc. cit. 34.
37. Biedl; loc. cit. 29.
38. Hammett, F. S., The effect of the maternal ingestion of desiccated placenta upon the rate of growth of breast-fed infants. Jour. Biol. Chem. (N. Y.), 1918, **36**, 569.
39. Rothschild, H. de, Bibliotheca Lactaria. Paris, 1904.
40. Göltz, E., Einflusz des Nervensystems auf die Vorgänge während der Schwangerschaft. Pflüger's Archiv. (Bonn), 1874, **9**, 552.
41. Ribbert: Archiv. f. Entwicklungsmechanik (Leipzig), 1898, **7**, —.
42. Pfister, M., Über die reflektorischen Beziehungen zwischen Mammae und Genitalia muliebra. Beiträg z. Geburtsch. u. Gynäk. (Wein), 1901, **5**, 421.
43. Halban; loc. cit. 27.
44. Hildebrandt, P., Zur Lehre von der Milchbildung. Beitr. chem. Phys. u. Pathol. (Braunschweig), 1904, **5**, 463.
45. Basch; loc. cit. 31.
46. Lederer, R., und Pribram, E., Der Einfluss von Plazentärextracten auf die Milchsekretion. Deutsch. med. Wchnschr. (Berlin), 1909, **36**, 2079.

47. Aschner, B., und Grigoriu, Chr., Placenta, Fötus, und Keimdrüse in ihrer Wirkung auf die Milchsekretion. Arch. f. Gynäk. (Berlin), 1911, **94,** 766.

48. Bouchacourt, M., Nouvelles rècherches sur l'opotherapie placentaire. C. R. Soc. Biol. (Paris), 1902, **54,** 133.

49. Niklas, F., Zur Frage der Plazentahormone und der Vermendung von Plazentasubstanzen als Laktagoga. Monats. f. Geburtsch. u. Gynäk. (Berlin), 1913, **38,** 60.

50. Mandl; Die klinische Bedeutung der Milchsekretion bei bestehenden Schwangerschaft. Wien. klin. Wchnschr., 1905, **18,** 73.

51. Lane-Claypon and Starling; loc. cit. 35.

52. Mackenzie, K., An experimental investigation of the mechanism of milk secretion with special reference to the action of animal extracts. Quart. J. Exper. Physiol. (Lond.), 1911, **4,** 305.

53. Gaines, W. L., A contribution to the physiology of lactation. Am. J. Physiol. (Balt.), 1915, **38,** 285.

54. Fieux, M. G., Contribution a l'étude du suc placentaire dans ses rapports avec la sécrétion lactée. Bull. méd. (Paris), 1903, **17,** 725.

55. Van Hoosen, B., The new method in obstetrics. Woman's Med. J. (Toledo), 1915, **25,** 269.

56. Cornell, E. L., Placental tissue as a galactagogue. Surg. Gyn. and Obst. (Chgo.), 1918, **27,** 535.

57. Van Hoosen; loc. cit. 55.

58. Cornell; loc. cit. 56.

59. McNeile, L. G., The effect of the ingestion of desiccated placenta during the first eleven days of lactation. A preliminary report. Am. J. Obst. (N.Y.), 1918, **77,** 377.

60. Hammett, F. S. and McNeile, L. G., The effect of the ingestion of desiccated placenta on the variations in the chemical composition of human milk during the first eleven days after parturition. J. Biol. Chem. (N. Y.), 1917, **30,** 145.

61. Hammett; loc. cit. 38.

62. Hammett and McNeile; loc. cit. 59.

63. Hammett, F. S., Variations in the composition of human milk during the first eleven days after parturition. J. Biol. Chem. (N. Y.), 1917, **29,** 381.

64. Van Hoosen; loc. cit. 55.

65. Hammett, F. S. and McNeile, L. G., The effect of the ingestion of desiccated placenta on the growth-promoting properties of human milk. Science (N. Y.), 1917, N. S. **44**, 345.

66. Cornell; loc. cit. 56.

67. Hammett; loc. cit. 60.

68. Hammett, F. S., The relation between growth capacity and weight at birth. Am. J. Physiol. (Balt.), 1918, **45**, 396.

THE INFLUENCE OF THE THYROID GLAND ON THE FORMATION OF ANTIBODIES

J. Koopman
The Hague (Holland).

It is a fact, well known to all workers of experience in carrying out Wassermann tests, that sometimes it is very difficult to get a hemolytic amboceptor with a high titer. There are rabbits which, after three or even after two intravenous or intra-abdominal injections of an emulsion of sheep red blood cells, give a serum with a good or even a high titer. From time to time, however, one may meet with a rabbit, well fed and apparently in good health, which may be injected "ad infinitum" without giving a serum with a sufficient hemolytic power. Though I have injected many rabbits I have never been able to tell beforehand whether or not the animal would produce a good amboceptor. I doubt if this is possible. In ordinary times what to do with a rabbit not producing an amboceptor of sufficient titer presents a simple problem. It may be used for all kinds of experimental work, but it is excluded for the Wassermann test.

During the last years of the war, rabbits were rare and expensive, and it is natural that the receipt of such a rafractory rabbit was considered a real calamity. I tried, therefore, to find a way to improve the amboceptor of such an animal. The formation of hemolytic amboceptor may be considered a special case of antibody formation. The formation of antibodies is a regenerative process. That regeneration is to a great extent under the control of the thyroid gland we know from the work of Hertoghe, Léopold Lévi and de Rothschild, Eppinger and Hofer and others. So the first time I encountered a rabbit which after 15 intravenous injections of 1 c.c. of a 5 per cent emulsion of sheep corpuscles gave a serum with a titer of 1:100, it was submitted to thyroid treatment.

At first intra-abdominal injections were made of fluid expressed from the fresh glands of the cow, and later on, as it showed itself more effective, of the pig. The rabbit weighed 3000 grams. In the beginning daily injections of a quantity of

fluid corresponding to a milligram of fresh substance were made and the dose gradually increased to 15 milligrams. Then when the animal began to lose weight and showed a diminished appetite, the dose was decreased to 10 milligrams daily. After some weeks the fluid was administered by mouth, using a Nelaton catheter No. 20 as a stomach-tube. After two months of treatment the amboceptor showed a remarkable increase of hemolytic power. When 1 c.c. of a 5 per cent suspension of sheep corpuscles was added to 1 c.c. of fresh serum of a guinea pig in a dilution of 1:20, 0.8 cc. of a dilution 1:1000 of the inactivated serum of the rabbit was enough to produce complete hemolysis. Before beginning the experiments the titer was 1:100; during treatment it increased to 1:1200. Though an amboceptor with a titer of 1:1200 is not ideal it could be used in the hemolytic system of the Wassermann test.

This male rabbit was put in a cage with a female with an amboceptor of 1:6000. Four young rabbits were born. When they were six months old, all were injected three times with sheep corpuscles. Three of them produced an amboceptor of a sufficient titer (1:3000; 1:8000; 1:3600). The fourth one, however, gave an amboceptor of only 1:150 which did not rise after 15 injections. Thyroid tabloids from a Dutch firm (Grana) were administered by mouth (one milligram of dried gland daily). After nine weeks of treatment the titer was raised from 1:150 to 1:2000.

During the administration of thyroid gland the injections of sheep corpuscles were continued. I cannot believe, however, that these injections were the cause of the formation of an amboceptor with a high titer. Both rabbits had been submitted to 15 injections of sheep corpuscles without any tendency to raise the hemolytic power of the serum. As soon as thyroid was given a gradual increase was seen in both cases. I am inclined to believe, therefore, that thyroid insufficiency had caused the low titer of the amboceptor.

I am quite aware that the last word in this matter has not been spoken. It is very possible that another rabbit would show the same symptoms, but caused by an insufficiency of another

gland or perhaps by the hyperactivity of an endocrine organ. At any rate it appears that endocrinology may open to serologists and bacteriologists a new field for investigation.

If not only the formation of hemolytic amboceptor, but also of agglutinins, antitoxins, bacteriolysins and other antibodies were included in such investigations an enormous field for research would be open. Almost nothing in this direction has as yet been done.

THE ACTION OF ADRENALIN ON THE KIDNEY

Frank A. Hartman and Ross S. Lang.

(From the Department of Physiology, University of Toronto)

Many investigators have studied the action of adrenalin on the kidney, both in regard to circulatory changes and to urine flow, and have found that one or both may be modified by this substance. Inasmuch as Cow (1) has shown that there is direct communication between the adrenal medulla and certain parts of the kidney, it appears that adrenalin might have some important function in the control of the kidney. In the present instance we have made a study of the influence of adrenalin on the kidney volume, both from gangliar and peripheral action. Although it is possible that adrenalin may influence urinary secretion independent of vascular changes, yet we know that if vascular changes occur they will also modify kidney activity. It is assumed that volume changes are due to vascular changes.

METHODS.

The methods employed were similar to those used in a previous study of the spleen (2), the kidney being enclosed in a gutta percha oncometer which was connected with a Brodie bellows recorder.

In the perfusions the vessels were all tied off and warm oxygenated Ringer's solution forced into the renal artery under a constant pressure. Injections of adrenalin into the perfusion fluid were made at the entrance of the perfusion cannula by means of a hypodermic needle piercing the rubber tubing. Passive effects of the injection were ruled out either by slow injection or else by a simultaneous removal of an equal quantity of perfusion fluid by another needle inserted farther back in the connecting rubber tube.

All animals were under the influence of ether. Adrenalin solutions were made by diluting Parke, Davis & Co.'s adrenalin chloride solution with distilled water.

RESULTS.

In an earlier research (3) we found that small doses of adrenalin injected into the general circulation caused constriction of the kidney, while in some instances larger doses caused

constriction followed by dilatation. Brief dilatation preceding constriction occurred at times, but appeared to be a passive result from a short rise in blood pressure.

Five more cats and three dogs were studied in this way, with results which agree with the earlier research.

One experiment may be cited. The kidney of a dog weighing 18 kgm. responded by constriction to doses of adrenalin ranging from 0.2 cc., 1:100,000 to 0.4 cc., 1:10,000. These were all depressor doses of adrenalin. The response to doses ranging from 0.4 cc., 1:10,000 to 3.0 cc., 1:10,000 was constriction followed by dilatation (Fig. 1); 0.6 cc., 1:10,000 was a depressor dose, while 1.3 cc. of the same dilution was pressor in effect.

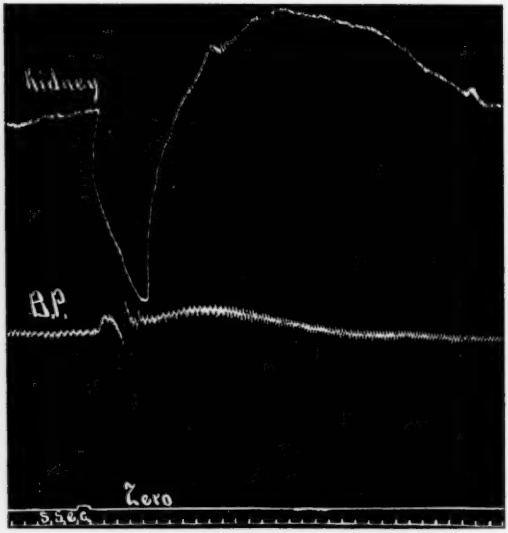

Fig. 1. Constriction and dilatation of a normal kidney from adrenalin, 1.3 c.c., 1:10,000 injected into the jugular vein. Dog 18 kgm.

Although this delayed dilatation occurring in the kidney was similar to that occurring in the intestines (3, p. 313), with large doses of adrenalin it was by no means so prevalent. However, in those individuals in which it was obtained it resulted repeatedly from injections above a certain dose.

We next attempted to locate the regions where adrenalin could produce these two effects, i. e., constriction and dilatation. In order to separate peripheral from gangliar or more central effects, we completely cut off the kidney from the body circulation, then perfused it. Nervous connections to the kidney were carefully preserved in the operation. Both kidneys were perfused alternately in two dogs. The first was an animal (18 kgm.) that gave constriction followed by dilatation of the kidney when its circulation was intact and a large dose of adrenalin was injected into the jugular vein. When perfused, the left kidney gave dilatations from jugular vein injections of doses above 0.2 cc., 1:10,000. Sometimes slight constriction preceded the dilatation (Fig. 2). Injections of adrenalin into the perfusion

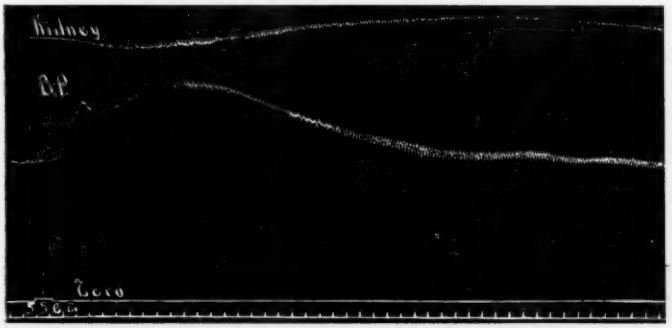

Fig. 2. Constriction and dilatation of a perfused kidney, 2 c.c., 1:10,000 adrenalin injected into jugular vein. Dog 18 kgm.

fluid caused a similar effect, i. e., constriction followed by dilatation (Fig. 3). Occasionally the dilatation was followed by constriction. The other kidney responded in a similar manner, both before and after perfusion.

The second dog (15 kgm.) gave dilatation in both perfused kidneys from adrenalin injected into the jugular vein, while injections into the perfusion fluid caused constriction (Fig. 4). Doses as small as 0.2 cc., 1:100,000 gave this result.

Volume changes in perfused kidneys from jugular vein injections of adrenalin, may be due to action on structures in the semilunar ganglion, dorsal root ganglia or in some more central location. We tried the effect of direct application of adrenalin to these

ganglia. The ganglia were usually slit to facilitate absorption. In the case of the semilunar ganglion, the mesentery was cut and separated from it in such a way that a pocket could be made

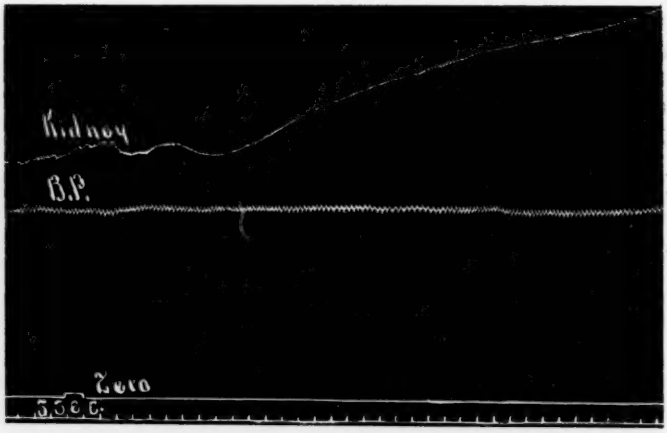

Fig 3. Constriction and dilatation of a perfused kidney from the injection of 0.2 c.c., 1:100,000 adrenalin into the perfusion fluid. Dog 18 kgm.

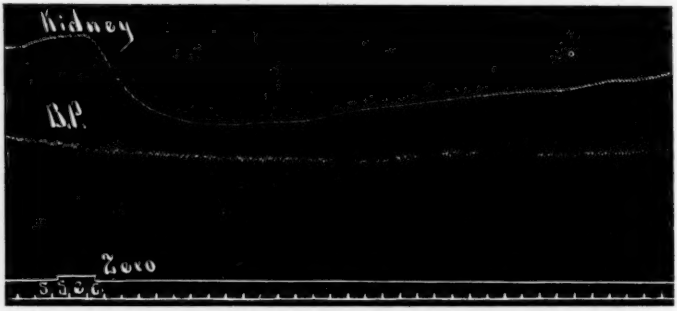

Fig. 4. Constriction of a perfused kidney from the injection of 1.3 c.c., 1:100,000 adrenalin into the perfusion fluid. Dog 15 kgm.

by engaging the cut surface of the mesentery with haemostats. Adrenalin solutions could then be confined in this pocket without absorption into the general circulation.

Adrenalin action on the semilunar ganglion was studied in three cats and one dog. Dilatation of the kidney was obtained in all of these when adrenalin was applied to the ganglion in question. In some animals, concentrations as low as 1:100,000 produced this result; in others a 1:10,000 solution was necessary (Fig. 5). In two of the cats the latter solution sometimes caused

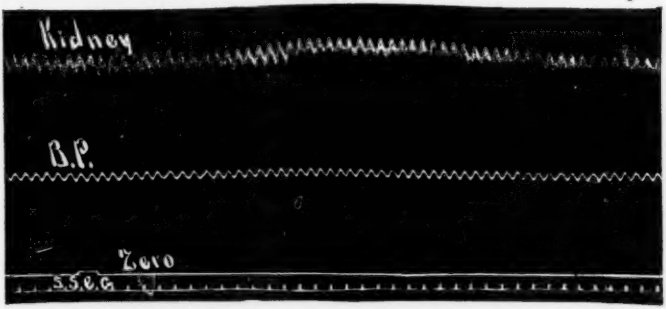

Fig. 5. Dilatation of the kidney caused by the application of 1:10,000 adrenalin to the semilunar ganglion. Cat. 3.1 kgm.

dilatation followed by constriction. This could be explained on the ground that small amounts of absorbed adrenalin affect the dilator mechanism, while larger amounts bring the constrictor mechanism into action. This was confirmed by the pure constriction which it was possible to obtain with concentrated adrenalin solutions (1:1,000) (Fig. 6).

We concluded from these observations that adrenalin can influence the volume of the kidney by action upon both dilator and constrictor mechanisms located in the semilunar ganglion, the result depending upon the concentration of adrenalin absorbed.

The effect of adrenalin through the dorsal root ganglia was studied in four cats. With the animal lying on its side, an opening extending transversely from the midline was made in the abdominal wall above the kidney. The kidney was placed in the oncometer and the apparatus properly adjusted before exposure of the dorsal root ganglia. The twelfth and thirteenth thoracic ganglia were carefully exposed and their connections with the spinal cord severed. After allowing a short time for the bleeding to stop, the adrenalin solution was applied to a ganglion. In

some cases, to make sure that adrenalin was not escaping into the general circulation, the ganglion was surrounded by rubber dam. The earlier the adrenalin was applied the more sensitive was the ganglion. In fact, if the ganglion had been exposed too long or the blood pressure had become extremely low, there was

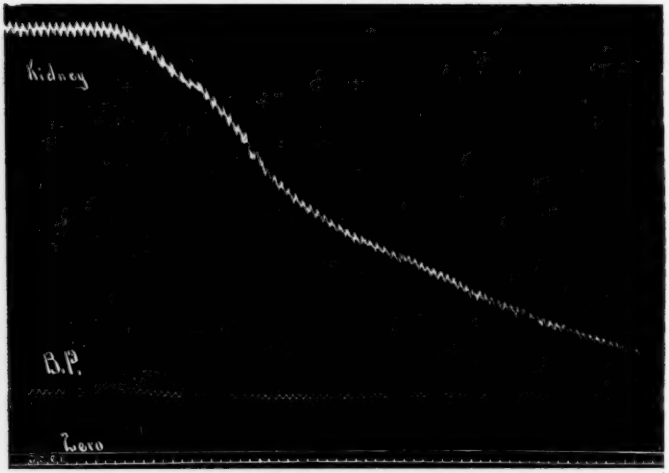

Fig. 6. Constriction of the kidney caused by the application of 1:1,000 adrenalin to the semilunar ganglion.

either no response or else only a slight effect. Second and third applications to the same ganglion had no effect unless several minutes intervened and the ganglion was thoroughly washed with isotonic salt solution. The adrenalin solution was warmed to 37° C. because cold solutions of distilled water sometimes produced an effect.

In one animal, constriction of the kidney was produced by 1:10,000 adrenalin applied to the dorsal root ganglia. No dilatation was obtained. The blood pressure, however, was quite low (32 mm.).

Dilatation of the kidney was produced in the three remaining animals from solutions of 1:10,000. One of these animals gave a similar response with 1:100,000 adrenalin. The response is frequently very slow, due no doubt to the slow absorption by the ganglion (Fig. 7).

Fig. 7. Dilatation of the kidney produced by painting a dorsal root ganglion with 1:10,100 adrenalin. The ganglion was surrounded by rubber dam. Cat 2.4 kgm.

DISCUSSION.

Our experiments prove that adrenalin frequently causes dilatation of the kidney. This dilatation can be caused by action on the semilunar ganglion, dorsal root ganglia, or, in some cases, on structures in the kidney itself.

Hoskins and Gunning (4) obtained dilatation following constriction in one dog out of sixteen from intravenous doses. This has been more frequent in our experiments, as five out of nine gave this response. In addition to these experiments, which were upon kidneys with an intact circulation, we have obtained dilatation of the perfused kidneys of two dogs.

Kidney dilatation from small doses of adrenalin may be more common than one might suppose. However, the constrictor mechanism in the kidney tends to predominate in adrenalin responses.

In view of the recent work of Addis, Barnett and Shevky (5) we tried to obtain dilatation of the kidney in a rabbit by the application of adrenalin to the semilunar ganglion. Concentrations of adrenalin from 1:100,000 to 1:10,000 caused only constriction in the kidney. This is confirmatory of recent work from this laboratory (6), which has shown that rodents are exceptional among mammals in that adrenalin vasodilator mechanisms are either absent or else insignificant in their action.

We also attempted to produce volume changes in the kidneys of cats by subcutaneous injection of adrenalin. Doses of 0.5 cc., 1:1,000 produced no distinct result. Three animals were tested in this way. Therefore, it seems that even in animals which are known to possess adrenalin vasodilator mechanisms subcutaneous injections have little effect upon the volume of the kidney.

In regard to the effect of adrenalin mingled with the perfusion fluid fed to a kidney, numerous observations have been made by others. Sollmann (7), with relatively large doses of adrenalin, obtained constriction. He says, however, that after several hours' perfusion, or sometimes earlier, the constrictor action disappears and that at times it is replaced by a dilator action. Pari (8) obtained one case of dilatation from adrenalin in the perfused kidney.

SUMMARY.

1. Adrenalin in moderate amounts produces dilatation of the kidney in some individuals.
2. Dilatation is usually preceded by a brief constriction.
3. Adrenalin can produce dilatation by its action on either the semilunar ganglion, dorsal root ganglia, or on some structure in the kidney.
4. Likewise constriction can be produced by adrenalin acting either in the semilunar ganglion, dorsal root ganglia, or the constrictor structures in the kidney.

BIBLIOGRAPHY.

1. Cow: The suprarenal bodies and diuresis; J. Physiol. (Lond.), 1914, **48**, 443.
2. Hartman and Lang: The action of adrenalin on the spleen; J. Pharm. and Exp. Therap. (Balt.), 1919, **13**, 417.
3. Hartman and McPhedran; Further observations on the differential action of adrenalin; Am. J. Physiol. (Balt.), 1917, **43**, 319.
4. Hoskins and Gunning: The effects of adrenin on the distribution of the blood; ibid., 1917, **43**, 304.
5. Addis, Barnett and Shevky: The regulation of renal activity; ibid., 1918, **46**, 39.
6. Hartman, Kilborn and Lang: Vascular changes produced by adrenalin in vertebrates; Endocrin., 1918, **2**, 122.
7. Sollmann: Perfusion experiments in excised kidneys; Am. J. Physiol. (Balt.), 1905, **13**, 246.
8. Pari: Action locale de l'adrenaline sur les parois des vasseaux et action des doses minimes d'adrenaline sur la pression du sang; Arch. ital. d. biol. (Pisa), 1906, **46**, 209.

ENDOCRINOPATHIC CONSTITUTIONS AND PATHOLOGY OF WAR*

N. Pende

From the Institute of Special Medical Pathology of the University of Palermo, Italy

The clinical study of the internal secretions opens a vast field of research, so far little known, notwithstanding its great value in practical medicine. Particularly important are those states of hormonic imbalance which are at the border line between health and disease, and which represent either latent or mild endocrinopathic conditions, real *endocrine diatheses* or *endocrinopathic temperaments.* It is already understood that for each of the best known endocrine glands, in addition to frank malfunctions there must be recognized minor degrees of perturbation giving rise to the endocrinopathic habitus.

To the French writers, especially Levi and Rotschild, we owe much of our knowledge of the hypothyroid habitus, and also, though not so thoroughly, the hyperthyroid; we owe to the American investigators, and especially to Cushing, a knowledge of the mild forms of hypo- and hyper-pituitarism; while the hypoadrenal constitution has been first studied in Italy (Constitutional angihypotony of A. Ferranini and the spurious hyposurrenalism of Castellino), as has also the hypogenital temperament (geroderma genitodystrophica of Rummo and Ferranini). In a way, however, the hypogenital habitus was described by Hippocrates, in case of the Scyti, who by being almost all the time on horseback developed signs of mild feminism in the males and of mild masculinism in the females.

The writer has been engaged for several years in the experimental and clinical study of the endocrinopathic habitus, and has found it quite as fruitful and interesting, practically, as that of the classic forms. Constitutional hormonic imbalance forms the pathogenetic substratum of a great many diseases, especially in the nervous and mental domain. It is of importance also in pathologic metabolism and growth, and in cardiovascular pathol-

*For an exposition of the theoretical conceptions involved in this paper, the reader is referred to a review of Prof. Pende's book, "Endocrinologia," published in this Journal, 1918, 2, 42-50.—Ed.

ogy. It plays a part in sexual perturbations and may also be a factor in infections, especially tuberculosis.

The War, in my opinion, showed clearly the importance of the constitutional hormonic anomalies in producing many slight disturbances of health, occurring every day, which represent the border line between health and disease. It has shown, furthermore, how such anomalies may lead to real disorders in sundry organs. Any endocrinologist who lived long among the soldiers had many opportunities to observe the close connection between various syndromes common in war life, and the endocrinopathic predisposition of the patients.

In this paper is summarized the results of my clinical observations during four years of war. These will be grouped as follows: (a) war syndromes, the most frequent and impressive, being the emotive-commotive psychoneuroses of the soldier; (b) the cardiovascular syndromes, often referred to under the inappropriate captions "irritable heart of the soldier" or "war heart"; (c) the relation of endocrine factors to infectious processes, and (d) the pathogenesis of "congelation" (torpor).

I. Endocrine Anomalies and War Psychoses.

By studying a great number of patients, suffering from acute psychoneuroses induced either by violent emotions or, oftener, by having been within the zone of explosion of large projectiles (commotive psychoneuroses), it is easy to recognize a complex of symptoms due to functional imbalance of the vegetative nervous system. These are often very slow to yield to treatment.

The most important of these symptoms, which in some cases constitute a clinical entity of "*diffuse sympathetosis,*" and in some what we could call a "*regional sympathetosis,*" are the following: mydriasis; wide open, anxious, shining eyes; diffuse tremor of the extended hands and Basedowian and Parkinsonian tremor; hyperidrosis, either diffuse or localized; rhythmic tachycardia (usually about 120 beats a minute); sometimes exaggerated and arhythmic or paroxysmal tachycardia; seldom a mild, nervous bradycardia, cured with atropin; pulsations of the superficial arteries; dermographism; vascular crises in the distal parts of the body (face, hands, feet), suggestive of symmetrical asphyxia of Raynaud; tricographism (Pende) and tricotonia; oculo-cardiac reflex usually absent or inverted, sometimes present; arterial pressure tending to increase, especially in the dias-

tolic phase; light hyperthermia or tendency to facile increase of the superficial temperature; rapid loss of weight; positive, though weak and dissociated, adrenalin reaction; seldom a slight spontaneous glycosuria; alimentary glycosuria; very seldom nervous vomiting; continuous or paroxysmal polyuria; hyper- and hypoperistalsis; hypotonia or spasm of the vesical sphincter; aphony or disphony; hiccough; asthmatic crises; diaphragmatic contracture and sudden and exaggerated gastro-intestinal meteorism. By analyzing with care these psychoneurotic syndromes the endocrinologist can recognize more or less definite forms of alterated endocrinism, though they are almost always attenuated.

This endocrine symptomatology is so closely connected with sympathetic symptomatology, that in such cases we can really say "sympathetic-glandular syndromes" or, as I have proposed to call them, "endocrino-sympathetic syndromes"; these acute war endocrinopathies show better than any other syndrome the close physiologic and pathologic synergy of these two trophic-regulating systems of our organism.

Chief among these syndromes is the status of *Basedowism*, which differs from the classical Graves' syndrome in the usually moderate tachycardia (90-120 pulsations a minute); the slight thyroid swelling; the almost constant lack of exophtalmos, while the eye is wide open and fixed and shining, and the great prevalence of tremors and muscular asthenia. It is very characteristic of this acute war Basedowism, of emotive-commotive origin, that it is likely to disappear readily in a few months after removing the patient to more quiet surroundings, or after a few applications of X-rays to the thyroid. I believe that its being mild and curable (at least in the majority of cases) is due to its *neurogenic* nature.

In this connection it may be stated that, clinically as pathologically, I divide all the endocrine syndromes into two principal types,—one chiefly *neurogenic* and the other chiefly *glandular*, according as the glandular dysfunction is a secondary symptom of alterated nervous influences, or is due to primary alterations of the glandular tissue. Thus we have Basedow, Addison or diabetic syndromes. There may be also pituitary, genital, thymo-lymphatic syndromes of neurogenic type. In these, besides the primary dominating pathogenetic factor of nervous nature (dynamic or organic alterations of the endocrino-secretory nerves),

the nervous symptomatology (true glandular neurosis) is a chief symptom. The course of the disorder, its oscillations and variations and its peculiar way of reacting to therapy show the characteristics of a neuropathy.

Any clinician of wide experience must recognize this nervous type of Basedow's disease. It is interesting in this connection to note that several pathologists (Wilson among the most recent) try to demonstrate a *nervous pathogenesis* of the disease, the thyroid alterations being regarded only as epiphenomena. Several observers, including the writer, have demonstrated also the existence of nervous forms of Addison's disease in which post-mortem examination failed to disclose any gross alteration of the adrenals.

As regards neurogenic diabetes, Von Noorden, more than anyone else, insisted during the war on the peculiar clinical characters of this type. This may be ascribed to the exaggerated action of glucomobolizing hormones, resulting from abnormal nervous impulses acting on the liver, pancreas and cromaffin system. Von Noorden regards this type as quite distinct from chronic pancreatic diabetes.

These neurogenic endocrinopathies often but not in every case differ from the endocrinopathies due to direct primary lesions of the glands, by their peculiar mildness, the uncompleted syndromes, their temporary character and their ready curability. The war gave rise to many instances of such clinical forms of dyshormonism.

Many observers studied the "war Basedowism." Among these are Rothacker, Stoney, Barr, Schulzinger, E. Romberg, Aschenheim, Ney, White, Hernaman-Johnson, Boschi and Pighini. The French observers, Sergent, Loeper, Oppenheim, Ramond François, Satre and Carles, studied mostly the "war Addisonism," and Von Noorden the "war diabetes."

It may be added that, besides the Basedowism, Addisonism and hypopancreatism, I saw rather often in soldiers exposed to intense psychic excitement, *genital symptoms*,—impotency, male chlorosis and gynecomastia,—rapidly developed.

Finally, very interesting are the cases of "mors thymica" which show at the post-mortem table status thymo-lymphaticus associated with hyperthyroidism. Two such cases have been seen by Pighini in two of our soldiers with "emotive-psychoneurosis";

three have been found by Schiboni, also in our soldiers; and all five, according to Pighini, demonstrate how the mental condition, if long lasting and associated with war fatigue, may determine, in predisposed subjects, a revivification of the thymus and of other lymphoid organs already involuted. This in its turn leads to the well-known dysfunctions: vagotonia; cardiac, respiratory and gastric disorders, and even sudden death.

So far we have not any unequivocal observations of hypophyseal reaction in the psychoneuroses of soldiers, though from some researches (especially the recent ones of Shamoff) there is reason to believe that the hypophysis secretion also is controlled by the sympathetic system, and hence is under psychic influence. Perhaps certain polyurias, suggestive of diabetes insipidus, and which we usually call either "spastic" or "nervous," might be an expression of alterated hypophyseal function. They are very often found, according to Rothacker, in the periods of the utmost psychic excitement.

There may here be recalled the observations, though few, of certain syndromes which seem to be connected, at least indirectly, with complex alterations of the endocrine system or, better, of the sympathetic-endocrine system. Dercum's syndrome, for instance, has been found sometimes in soldiers undergoing intense emotions. Two such cases have been described in Italy, one by Alzona and the other by Bochi, who found several symptoms of hypophyseal hypofunction. The neurofibromatous syndrome of Reklinghausen has been reported by Roccavilla, Guillain and Barré as developing in some soldiers under the influence of the war.

The frequent occurrence of syndromes of hormonic imbalance due to war emotions is no doubt connected in some instances with a condition of constitutional instability of the endocrine glands, so that these may easily be either excited or inhibited by nervous impulses. The same unsteadiness in the toxi-infective processes of the soldiers will be discussed in a later section.

My researches on the habitus of subjects stricken by these syndromes lead to the conclusion that the most predisposed are the patients with hyperthyroid status, more or less pure, i. e., more or less associated with stigmata of lymphatism or of constitutional hypoadrenalism.

In such temperaments "sympathicotonia" generally prevails

and may be associated or alternated with "vagotonia" whenever the hyperthyroid function is accompanied by status lymphaticus or by hypoadrenalism. I believe that in determining the psychoses of war a lack of resistance of the endocrine-sympathetic system is the most important pathogenetic factor and the one, besides, that explains the peculiar features of these various syndromes (hypersthenic forms when hyperthyroidism predominates and asthenic and depressive when hypoadrenalism prevails).

Recently Buscaino has insisted on the importance of the endocrine-sympathetic habitus (especially hyperthyroid) in a class of neuropathic soldiers which he calls *constitutional kinesthopathic*. Bratz refers to them as affected by *emotive epilepsy* and Dana calls them "psycholeptic." These soldiers are easily subjected to kinesthetic alterations, to outbreaks of furious rage, during which they are apt to commit acts of insubordination or violence, associated or not with a state of semi-consciousness (never with total unconsciousness) or with crises of motor excitation. These subjects also, according to my findings, show predominance of hyperthyroid habitus.

Nowadays several psychiatrists especially interested in the study of war psychoneuroses admit that steady and repeated psychic traumata connected with the war have determined, in predisposed individuals, a sort of *neuropsychic anaphylaxis*, a thesis developed by Boschi and Bennati in Italy and by Roussi and Lhermitte in France. I believe that such neuropsychic hypersensibility to psychic, physical or chemical stimuli is brought about essentially by the abnormal action of the hormones on the nervous centers. The thyroid hormone (according to Cannon also the cromaffin hormone) may easily be increased through psychic exciting influences, and sensitize the nervous centers, especially those of the vegetative life; other hormones, i. e., the parathyroid, which under normal conditions are supposed to moderate the neuropsychic excitability, may perhaps undergo a diminution or an inhibition through long lasting and violent psychic influences, which condition also leads, by another road and in combination with hyperthyroidism, to a neuropsychic hypersensibility.

We may mention, also, in this connection Léopold Lévi's opinion that paroxysmal hyperthyroidism and functional instability of the thyroid have great pathogenetic importance in deter-

mining the anaphylactic syndromes of "neuro-arthritism," and in determining paroxysmal endocrine hypersecretory crises. These he calls "Endocrinolepsies."

We believe that hereafter the constitutional imbalance between the thyroid and parathyroids, i. e., hyperthyroidism combined with the hypoparathyroidism, must be held as the key to these conditions of "neuropsychic anaphylaxis." The frequency of spasmophilia, of mechanical and electrical neuromuscular hyperexcitability, of vascular spasmophilia (vasomotor epilepsy of Bratz) observed in soldiers affected by acute psychoneuroses (Pighini, Buscaino) suggest a status of parathyroid inhibition which, I believe, is often associated with the thyroid hyperfunction.

II. Constitutional Endocrine Anomalies and "Soldier's Irritable Heart."

Having had a chance to study many soldiers showing nervous and functional cardiac weakness, I have been able to distinguish four principal types of "irritable heart." Such forms are not absolutely distinct from each other; sometimes they can even be associated or alternated in the same patient, but, in the pure cases, they cannot be grouped in a single category, either as to their pathogenesis or their prognosis and therapy.

A first clinical type, which we may call "thyroid, sympathicotonic or Basedowiform heart," presents the cardiovascular symptoms very much like those of the initial or mild forms of Graves' disease. As regards such cases we can really admit with White and Hernaman-Johnson that the irritable heart is a "sort of pre-Graves condition." Quite pronounced in these patients is the thyroid habitus, characterized usually by lean body or tendency rapidly to become thin through psychic causes. They have clean cut features, thick hair, often wavy or curly (Pende's tricotonia); thick and long eyebrows; large eyes, open, lively, shiny, bright, sometimes with nystagmic motions, and well differentiated sexual traits. Often there is hypertricosis of the face and of the whole body; teeth and nails very well developed; skin rich in pigment, especially in the palpebral region and at the extensor surface of the hands and increased pigmentary reaction to external stimuli. These patients often show also a symptom, which I described in hyperthyroidism, i. e., hyper-

excitability of the muscles arrectores pilorum to mechanical stimulation or *tricographism.* The thyroid may or may not be slightly enlarged. Their blood shows mononucleosis, especially of the Pappenheim leukoblasts.

Even before the development of their illness, such individuals usually have shown in some degee the functional characteristics of hyperthyroidism, i. e., a functional *juvenilism, a tachypragia* corresponding to the somatic juvenilism, motor and psychic restlessness, agility, tachyphagia, intestinal hyperperistalsis, cardiac acceleration on the least provocation, pulsation of the arteries, crises of hyperidrosis, great emotivity, unusual quickness of perception and volition, impulsiveness and peculiarly explosive personality. To these characteristics of the hyperthyroid temperament correspond rapid and precocious growth. Owing to a marked tendency to catabolism, especially of protein, habitual leanness and crises of muscular and psychic asthenia are common.

The cardiovascular phenomena induced by the war on this hyperthyroidic substratum are usually sympathicotonic. There is continual tachycardia, almost always moderate (100-120) though of a changing ratio and accompanied by painful pulsating sensations, but very seldom by real paresthesia and pains of the heart. There are at times, however, hyperalgesic zones (Head) to the left of the chest and of the neck.

The tachycardia is generally rhythmic (sinus type); extrasystoles are almost never found. The heart at times has a rounded apex and moderate hypertrophy of the left ventricle. The aorta may be in a condition of temporary atonic dilatation, but functional souffles are very few. The oculo-cardiac reflex is either very moderate or absent or inverted (sympathicotonic). Tonic reflex contraction of the cardiac cavity under stimulation of the precordial region is easily elicited. There are frequent angiospastic phenomena at the distal parts of the body. Diastolic pressure is slightly increased, due to hypertonia of the peripheral arteries. The functional capacity of the heart varies greatly, especially in accordance with the psychic conditions, leading to frequency of sudden and unexpected crises of myocardial exhaustion; these are rapidly transitory most of the time—a sort of functional claudication of the heart.

This clinical form of "soldier's heart" is found mostly in sol-

diers exposed to violent and long lasting cannonading, or within the zone of explosion of large projectiles, or with a slight febrile rheumatic infection, which often starts the cardiac disturbance. Very often there is no cardiac trouble in their anamnesis. We may admit that the repeated emotions or a violent physico-psychic shock (explosion of large projectiles) or the rheumatic virus can easily bring about a frank Basedowism in one of hyperthyroid constitution, having a thyroid already tending to hypersecretion. Such Basedowism may be of a type predominantly cardiovascular, predominantly neurogenic, or thyreotoxic; in all these cases, however, cardiovascular sympathicotonic phenomena are particularly in evidence.

A second clinical type of "soldier's heart," less frequent than the preceding one, shows essentially those heart disorders which Eppinger and Hess described in the vagotonic constitutions. In such individuals the stress of war frequently leads to frank vagotonia.

Peculiar to these people are the stigmata of adenopathy and sometimes also signs of organic immaturity and of infantilism. A slight degree of thyroid swelling, of hypertonia and retraction of the upper lid, of shining and protruding eye bulbs, of fine muscular tremors and of nervous and psychic irritability, bring these people near to the true thyroidism (vagotonic hyperthyroidism or lymphothyroidism).

The cardiovascular reactions of these subjects differ in many ways from those of the first class. There is arhythmia of the extrasystolic, the respiratory or the juvenile types; there is no tachycardia at rest, but, on the contrary, slight bradycardia. This in some cases through the least strain or psychic excitation may turn into an even severe tachycardia, which, however, is temporary and ends in bradycardia. The apex beat is often rather lively and diffuse; the region of the pulmonary artery may appear pulsating; sometimes the heart is very movable. There are very severe cardiac paresthesias, very distressing to the patients. Frequent and sometimes intense and lasting functional souffles are heard. The oculo-cardiac reflex is always present and accentuated. Red dermographism is a constant finding associated with a rather low diastolic and an increased pulse pressure.

This type of "soldier's heart," of a vagotonic form, has

been found by other authors (Hirtz, Gouget, Binet, Petzetakis, Braun and Von Dzyembowski). We believe that to this type belong the people with prevailing "vagotonic hormones," though they are not yet well known nor chemically differentiated. Eppinger and Hess found in these vagotonic patients hyperplasia of the thymus, the same as is found in cases of Basedow's disease with pronounced symptoms of vagotonia.

In a third clinical type of "soldier's heart" the syndrome appears like a true myasthenia cordis, while in the two preceding forms one could speak of "neurasthenia cordis." In this third class, there is the well known asthenic constitution of Stiler, or better, asthenic hypoplastic (Bartels), in which, according to my observations, constitutional hypodrenalism dominates. This is very often associated with hypopituitarism and hypogenitalism.

The hearts of these patients are small and hypoplastic (the "cuore a goccia"—globular heart—of the Italians); the cardiovascular syndrome, which the war makes conspicuous, amounts to a true insufficiency of the heart to any strain, a real cardiac myasthenia associated with symptoms of nervous and psychic irritability and weakness, which characterize their temperament. As well for the vagotonic heart, as for the hypoplastic-asthenic heart, the cardiac anomalies have not been created by the war, but only exaggerated.

There is a fourth group of functional cardiopathies in men who before the strain of military service never showed any insufficiency of the heart nor any constitutional anomaly. These occur in rather elderly soldiers called back to the colors, who, out of fear of the war, even without having been exposed to the exertions and the intense emotions of trench life, show general adynamia and cardiovascular phenomena so severe as to lead us to think of a true myocarditis. They display palor of the face, cyanotic lips, atonic and sunken eyes, livid and cold extremities, sometimes slight edema of the lower limbs, peripheral hypothermia, anorexia, dyspnea, absolute physical prostration to the extent of not being able to sit up in bed, severe psychic depression and rapid cachexia. The heart is at times of an increased size with weak and muffled tones associated with moderate bradycardia and diminished systolic and diastolic pressure. They are not amenable to any treatment, but they recover rapidly as soon as removed from the military life.

In these cases one is apt to think of hypoadrenalism and we can accept the hypothesis of a functional inhibition of the adrenals due to the war, followed by a pseudo-myocarditic syndrome, as seen in some forms of adrenal insufficiency through organic alteration of the glands.

The neuropsychogenic origin of the adrenal insufficiency of these patients, which must obviously come from a certain instability of the glands or from an easy exhaustion of their secretory nerves, explains the peculiar clinical characters of this form and its easy curability by the removal of its psychic causes. Cases of such form, which we may call "hypoadrenal types," have been observed by other authors, e. g., by Satre at the French front. He claims that such cases may be taken for neurasthenia, or sometimes peritonitis, dyspepsia, tuberculosis, or latent carcinomatosis, according as there is found headache and asthenia, abulic depression or Hippocratic facies with abdominal pains, dyspepsia or cachexia, respectively. But Satre does not mention the peculiar myocarditic syndrome that may be found in some of these patients.

III. Constitutional Endocrine Anomalies and Infections.

Of all the endocrine glands the adrenals are the oftenest affected in the course of infections such as epidemic infectious icterus, typhoid and paratyphoid, malaria, dysentery and other infections with unknown organisms. In this way we can explain the syndrome of hypoadrenalism described in soldiers suffering from infectious icterus in Italy by Frugoni, Gardeghi, Ancona, Notari and Monti; from typhoid by Frugoni, Oppenheim and Loeper; from dysentery by Izar, Dujarric, Riviere and Fillerval; from malaria (severe) by Paisseau and Lemaire and from indefinite infections by Carles and Satre. Even anti-typhoid vaccination evoked in some predisposed subjects signs of acute adrenal insufficiency (Loeper).

The adrenal symptoms in these infections are no doubt accentuated, in their initial stages, by the capsular exhaustion due to the excessive war fatigue (Sergent) and, we may add, the adrenal exhaustion due to long felt emotions, as demonstrated by Cannon and his collaborators. To explain such adrenal insufficiency of war we must admit a glandular weakness already preexisting and due to constitutional conditions.

One way in which constitutional imbalance of the endo-

crine glands has, to my knowledge, an important predisposing influence in the infectious pathology of soldiers is in preparing the ground for the so-called war tuberculosis.

During more than a year's service directing the diagnostic center for the tuberculous soldiers of the XII Corps of the Italian Army, I had a chance of studying thoroughly, from the endocrine point of view, a great many soldiers in the several stages of consumption. Confirming the results of my previous researches on the relation between endocrine glands and tuberculosis (N. Pende: Organi endocrinici e tubercolosi. Il Morgagni 1912 No. 45-46), I found that the war tuberculosis is seen especially in those subjects who show constitutional hormonic imbalance; that is, in the first instance, in patients with hyperthyroid-hypoadrenal habitus; and in the second place in patients with either hypogenital habitus or thymo-lymphatic status. Signorelli, confirming my views as to the marked predisposition to tuberculosis in these hyperthyroid-hypoadrenal individuals, has called attention to the special facies characteristic of war tuberculosis. This is to be ascribed to the endocrine condition just mentioned.

It is probable that the great number of cases of mild tuberculosis, especially of the lymphatic glands and of the serous membranes, found by me in soldiers back from the front, may be related to the status lymphaticus and status thymo-lymphaticus found in many returned soldiers. Doubtless the adrenal hypoplasia and thyroid hyperplasia associated with persistent thymus also play a part. To this may be added also a secondary form of hypogenitalism often to be found in the soldiers.

We finally know, through the researches of Von Noorden, how often hyperglycemia occurs in soldiers exposed to the fatigue and stress of war. This is probably due to pancreatic deficiency resulting from infections. This hyperglycemia also predisposes the subject of tuberculosis.

IV. Hormonic Anomalies and Torpor.

V. Neri, in Italy, found in many soldiers with torpor of the extremities sluggish vasomotor reactions, analogous to those of hypothyroidism; hence he proposes as a preventive treatment thyroid opotherapy.

In such cases I have found associated hyperthyroidism and vagotonia manifested by angioecstatic phenomena (exaggerated

red dermographism) and by a certain degree of permanent acrocyanosis of the distal parts of the body.

CONCLUSIONS.

The "war endocrinology," studied from the point of view of the predisposing action of the individual hormonic anomalies towards the various groups of morbid conditions in the soldiers, demonstrates, even better than in time of peace, how great is the importance of the *endocrine temperaments* not only in the pathogenesis of the endocrine syndromes *sensu strictiori*, but also of the nervous and mental affections, of the cardiovascular morbid conditions, of some infectious processes, especially tuberculosis, and of some trophoneurotic and angio-trophoneurotic affections.

Two forms of dyshormonism chiefly are found in the war pathology, one prevalently hyperthyroid and the other hypoadrenal.

The thyroid and the adrenals are the most easily influenced by psychic factors. The extraordinary influx of psychic disturbances on the body life, especially in the field of the vegetative nervous system, is the factor that gives its peculiarity to the morbid syndromes of the soldiers, no matter of what kind they are. Such morbic reaction very likely depends upon a chain of psycho-somatic relations, of which the thyroid and the adrenals, and possibly other endocrine glands, are indispensable links.

BOOK REVIEW

"THE INTERNAL SECRETIONS AND THE NERVOUS SYSTEM." Dr. M. Laignel-Lavastine. Authorized Translation, Translator's Preface and Introduction by Dr. F. B. Robeson. Nervous and Mental Disease Publishing Co., New York and Washington, 1919, pp. 57.

Although dated 1919 the book, as a matter of fact was written in 1914, and hence does not include any of the work of the past five years, and especially that dealing with war neuroses. Much of the subject matter is based directly on the observations of the author, but a bibliography, largely French and German, of some 150 titles, is also utilized.

The difficulties of writing acceptably upon a topic of which so little is known are recognized and engagingly emphasized. For the most part only tentative conclusions are reached and the way is pointed for many more researches. While it must be recognized as the author maintains, that there is some sort of reciprocal relationship between the endocrine and nervous systems, "from a pathological standpoint, much less is known than one would suppose."

The first section of the monograph is devoted to a seriatim discussion of "Nervous disturbances in the endocrine syndromes" outlining both the "uniendocrine" and the "polyendocrine syndromes." This is followed by a section on "Endocrine disorders in nervous syndromes." These include sensorymotor, vegetative and psychic syndromes. The last twenty pages are devoted to an "Endocrine-neurological sketch" in which such topics as Asthenia, Headache, Insomnia, Anxiety, Sweats, Constipation, Arterial Hypertension, Obesity and various "Endocrine-sympathetic syndromes" figure. The Psychoneuroses are also treated. It is in the study of such topics as these that the author believes Endocrinology is of greatest aid to the neurologist.

The book is written by and for neurologists who are assumed already to have a considerable command of the subject matter. Such readers will find it an interesting attempt to organize in brief scope a large amount of information. The general reader will find it rather too technical and concentrated to be easily followed.—R. G. H.

ABSTRACTS

ADRENAL dyspepsia. (La dyspepsie surrénale.) Loeper, Beuzard and Wagner. Prog. Méd. (Paris), 1917, **32**, 241.

Of the group of dyspepsias secondary to endocrine disturbance one can isolate a suprarenal dyspepsia due to capsular insufficiency, and manifested by atonicity and coprostasis. Suprarenal insufficiency should be suspected in a large number of gastropathic and constipated conditions observed in fatigued soldiers. Inefficacious medication should be replaced by adrenin injections.—F. S. H.

(ADRENAL) Adrenopathic hyperchlorhydrias. An endocrine therapeutic study. Kaplan (D. M.) and Greeff (J. G. W.) N. Y. Med. J. (N. Y.), 1919, **108**, 61.

A report of three cases of gastric disturbance greatly relieved or cured by the use of suprarenal gland extract.—H. W.

(ADRENAL) L'hypertrophy et la teneur en adrénalin des surrénales dans les infections, les intoxications et certains états d'immunité. (The hypertrophy and adrenalin content of the suprarenals in infection, intoxication and certain immune states). Porak (R) J. Physiol. et. Path. Gen. (Paris), 1918, **18**, 95-112.

Various animals were infected with rabies, tetanus, poliomyelitis, diphtheria or pneumonia; poisoned with lead, mercury, strychnine or chloroform; subjected to the action of the endogenous toxins produced by insomnia or nephritis, or to continued injections of adrenalin. Under these pathological conditions no constant relation was found to exist between the arterial pressure and the adrenin content of the suprarenal glands, the latter being determined by injecting extracts into rabbits and dogs and noting the extent of the rise in blood pressure. However, the ratio of the body weight to the weight of the adrenal glands (dried at 56° C.) was frequently found to be modified, especially if the diseased condition had been long continued. The body weight decreased, the glands (particularly the cortex) hypertrophied, and the pressor action of the

extracts was diminished. The author emphasizes the fact that the function of adrenalin is not to maintain the tone of the blood vessels, and that the fall in arterial pressure often seen in pathological conditions is not due to a loss of adrenin from the circulation. The changes occurring in the suprarenal glands in these states are largely in the cortex.—L. G. K.

(ADRENAL) The postnatal development of the suprarenal gland and the effects of inanition upon its growth and structure in the albino rat. Jackson (C. M.), Am. J. Anat. (Phila.) 1919, **25**, 221-291.

A volumetric and histological study of the gland in 108 rats, including normal organogenesis and histogenesis; volumes of cortex and medulla, of parenchyma and vascular stroma, and of cytoplasm and nuclei; occurrence of mitosis; effects of stunting by underfeeding the young and effects of acute and chronic inanition upon the adult. Confluence of the medulla, with absorption of the intermixed cortical strands, occurs during the first week. Expansion of the medulla continues, with absorption of the cortex at the inner zone and regeneration from the outer zone. The cortex in general increases in relative volume, with no apparent sexual difference and no marked change during inanition. The vascularity in general increases from the periphery toward the center, with variable increase during inanition. During inanition there is a variable amount of cellular atrophy, especially in the middle cortical zone, and increased degeneration in the inner zone. The medulla is less affected. Mitosis (in the young) is prevented, but is rapidly reestablished upon refeeding. In stunted young rats the normal differentiation of liposomes continues, especially in the outer cortical zone, with pigment formation in the inner zone. In adult rats the liposomes resist inanition remarkably, especially in the outer zone, where they persist nearly unchanged. In extreme cases they disappear from the remainder of the cortex. The chromaffin reaction is weak in young rats and may be diminished by extreme underfeeding. In adults it is (aside from post-mortem changes) apparently unaffected by inanition.
—Author's Abstract.

(ADRENAL) The relative volumes of the cortex and medulla of the adrenal gland in the albino rat. Donaldson (J. C.) Am. J. Anat. (Phila.), 1919, **25**, 291-299.

The measurements for this study were made on the adrenal glands of seventeen albino rats fixed in Bouin's solution and reconstructed from serial sections. The left adrenal is usually distinctly heavier than the right. The relative volume occupied

by medullary tissue decreases from about 12 per cent for the males and 10 per cent for the females at birth to 7.5 per cent and 6.5 per cent, respectively, at about the time of puberty. From this time on there is relatively little change. When compared with those of the male, the glands of the female, body weight for body weight, contain relatively less medulla.

—Author's Abstract.

ADRENAL GLAND, Primary tumor of the—. (Neuroblastoma Sympathicum). Wolbach (S. B.) and Morse (J. L.), Am. J. Dis. Child. (Chgo.) 1918, **16**, 63.

The authors report a case of a primary tumor of the left adrenal gland in a boy 4 years and three months old. At necropsy metastases were found in the liver, but nowhere else. The symptoms of the overgrowth of the liver overshadowed all other signs. Notes are added on two other cases, one in a boy aged 7 months and another in a girl of two years. Their three cases bring the number of undoubted cases of neuroblastoma sympathicum to twenty-nine thus far reported, twenty of which were primary in the adrenal gland. The others have taken origin in sympathetic ganglia (3), retroperitoneal tissue (3), coccygeal gland, nose and uterus. The literature on the subject is briefly reviewed.—M. B. G.

(ADRENALS) Addison's disease. Gottheil, J. Cutan. Dis. inclu. Syph., 1916, **34**, 224. Society transactions.

A man 40 years old who had suffered a three months' attack of eczema returned to the hospital for further treatment. He showed a slight degree of eczema, a little thickening of the skin and moderate itching. The skin was dark in color. Although no demonstrable pathology could be demonstrated, the patient developed general debility and further bronzing of the skin. The pigmentation involved the entire skin, but was most marked on the legs. The eczema cleared up on treatment. Suprarenalin medication did not affect the coloration.—H. W.

(ADRENALS) A opotherapia suprarenal e as suas multiples indicacoes. (Adrenal organotherapy and indications for its use.) Franca Rocha (A.) Archivos de Biologia de San Paulo (Brazil), 1918, **3**, 411.

General review of the uses of adrenalin in medical practice and a discussion of dosage. No new data.—G. P. G.

(ADRENALS) Contribution a l'étude du fonctionnement de la capsule surrènale humaine a l'état normal, et dans les

états infectieux en particulier dans les gangrênes gazeuses. (Function of the human adrenal cortex in normal condition and in infections, particularly gaseous gangrene). Goormaghtigh (N.) Arch. méd. expérimentale (Paris) 1918, **28,** 277.

An extended study of the morphology of normal and pathological adrenals led to the conclusions that each zone of the cortex has a certain specific function, and that the infections of a gangrenous type accompanied by gas formation cause a liberation of a considerable amount of cholesterol and chlosterol esters into the blood stream with consequent disturbances of function.—F. S. H.

(ADRENALS) De l'activité fonctionnelle de la gland medullaire surrènale des tuberculeux. (Functional activity of the adrenal medula in the tuberculous). Porak (R.) Ann. Méd. (Paris), 1918, **5,** 404.

In four cases of tuberculosis clinically quite unlike, it was noticed, in trying the functional activity of the suprarenal extract, that there occurred a persistency of the hypertensive effect. The immediate effect gives the determination of the proper dose. The rising of the lowest pressure during a series of injections of suprarenal medullary extract is a very important symptom showing that the treatment must be stopped.
—F. S. H.

(ADRENALS) On the functional relations of the suprarenal gland and the retinal pigment. Arey (L. B.), Anat. Rec. (Phila.), 1919, **16,** 138.

The influence of extremes of temperature on the position of the visual cells and retinal pigment of dark-adapted anuras differs both in degree and kind from that exhibited in other vertebrates. In the frog these temperature changes are of maximal order—such as have been associated chiefly with light adaptation. This unusual response may conceivably depend either upon direct nervous control or on hormone activation.

Controlled experimentation proves that adrenalin is able to induce, for example, maximal pigment expansion in the frog. Extracts of other endocrine glands fail to exert a similar influence. On the contrary, certain other observations are suggestive of nervous control.—Author's Abst.

(ADRENALS) La fonction des surrènales. Gley (E.) et Quinquaud (A.) Arch. néerl. de physiol., 1918, **3,** 1-6.

Data published elsewhere. See Endocrin. **2,** 473.

(ADRENALS) Influenza and suprarenal glands. von Tiling (H. M. A.), N. Y. Med. J. (N. Y.), 1918, **108**, 895.

Certain influenza patients present almost the classical symptoms of Addison's disease, extreme muscular weakness, tendency to syncope, insomnia, low diastolic pressure with high pulse pressure and pigmentation of the skin. In the author's experience the administration of repeated injections of epinine and adrenalin chloride solutions in such cases was followed by marked improvement. The severe backaches so often complained of usually cleared up on the administration of epinine. Such observations give the impression that the administration of suprarenal substance or epinine sustains the patient during a period of suprarenal gland exhaustion.—H. W.

(ADRENALS) Report of a case of Addison's disease. Hall (G. R.), Hosp. Bull. Dept. Pub. Char. (N. Y.), 1917, **1**, 39-42.

A complete clinical description of a patient having Addison's disease. Treatment with adrenin gave indeterminate results.—F. S. H.

(ADRENALS) Suprarenal syndrome in paludism. Fraga (C.), Trans. Am. Soc. Trop. Med. (N. Orleans), 1917, **11**, 39.

A report of a case diagnosed as suprarenal form of paludism showing intense muscular asthenia; deep adynamia; hypothermia; weak, unstable, irregular pulse; disturbances of digestion, etc. The blood showed the presence of Lavaran's parasites. Opotherapy was beneficial and the patient discharged cured.—F. S. H.

(ADRENIN) Action de l'adrénaline sur la motricité et la contractilité gastriques. Pron (L.), Bull. gén. Therap. (Paris), 1918, **170**, 86.

The administration of adrenaline in atonic conditions of the gastric musculature gives marked relief.—F. S. H.

ADRENIN, Dosage and method of administration of—(Posologie et mode d'administration de l'adrenaline). Sergent (E.), J. de med. et chir. prat. (Paris), 1917, **88**, 753-760.

Sergent considers that the commonly prescribed dose of adrenin is too small and advocates larger doses varied according to the case, the desired effect, and the mode of administration. Adrenin is indicated in two general classes of disorders—suprarenal insufficiency and morbid conditions wherein the physiological properties of the drug are of therapeutic value.

In acute suprarenal insufficiency 5-6 mg. by injection per 24 hours is not too much; in cases unaccompanied by gastric disturbances four capsules of 3 mg. desiccated suprarenal substance a day are preferable. In the chronic types the ingestion of 3 mg. of the dried material plus the injection of 2 mg. of the extract is beneficial. In asystolic conditions where digitalis is ineffective and also in tuberculosis of the adrenals, the injection of .5 mg. adrenin per day is indicated. The drug should always be administered in fractional doses at regular intervals throughout the twenty-four hours, with at least two hour intervals, no matter what is the method of administration. The injections should never exceed 0.5 mg. at any one point, though as much as 2 mg. can be given at one time.—F. S. H.

(ADRENIN) Experimental studies on the anaphylaxoid of salvarsan. Hirano (K.) Proc. Japanese Bacteriol. Soc. (Tokyo), 1918. Abst. of Bacteriology, **2**, 324.

Confirming the work of Milian, H. showed that the anaphylaxoid of salvarsan may be prevented by the injection of adrenaline. The intravenous injection of salvarism and neosalvarsan reduced the quantity of adrenaline in the suprarenal and in the blood. This reduction is transitory. Chem. Abst., **13**, 1229.

(ADRENIN) L'adrénaline dans la prophylaxie et le traitment de la réaction á l'injection de collobiose d'or. (Prophylactic use of adrenalin preceding colloidal gold injections). Rosenthal (G.), Bull. gén. Therap. (Paris), 1918, **170**, 80.

The congestion and tremors attending the therapeutic use of colloidal gold are markedly reduced when preceded by the administration of adrenaline.—F. S. H.

(ADRENIN) Ingestion d'adrénaline et injection intraveineuse de quinine. Rosenthal (G.) Bull. gén. Therap. (Paris), 1919, **170**, 412.

The ingestion of one to two milligrams of adrenaline in solution twenty minutes before the intravenous administration of colliodal quinine prevents the disturbing effects of the latter, observed when it is used alone.—F. S. H.

(ADRENIN) L'ingestion d'adrénaline dans la suppression de la réaction á l'injection intraveineuse d'or colloïdal. (Suppression of reaction to colloidal gold by adrenalin ingestion). Rosenthal (G.) Bull. gén. Therap. (Paris), 1919, **170**, 414.

R. found that if he fed 1 mgm. of adrenalin in solution twenty minutes before the intravenous injection of the colloidal

gold, the subsequent shock was largely averted. When more than 1 c.c. of colloidal gold is used 2 mgm. of adrenaline is indicated. Under ordinary conditions the adrenal secretion suffices to maintin arterial pressure even during an infection, but on the intravenous administration of the colloidal gold solution it becomes very weak, not as an actual insufficiency but due to a lessened activity, a meiöpragia, which is combatted by the preliminary ingestion of adrenaline.—F. S. H.

ADRENIN glycosuria, Influence of diet upon—. (Zur Kenntnis der Einflusses der Ernährung auf die Suprarenin-glykosurie). Biberfeld (J.) Arch. f. experimentelle Path. u. Therap. (Leipsic), 1919, **84**, 360.

A meat diet inhibits glycosuria produced by adrenin injections, but augments that caused by inhalation of carbon monoxide. Bernard's piqure glycosuria cannot be explained as due to adrenin discharge because the glands never produce enough to evoke such a reaction.—J. K.

(ADRENIN) Osteomalacia (Über gehäuftes Auftreten von Osteomalazie und eines osteomalazie—ähnlichen Symptomenkomplexes.) Edelmann (A.) Wien. klin. Wchnschr., 1919, **32**, 82.

In a short period 19 cases of osteomalasia were seen in nonpregnant women. The changes in the pelvis were relatively less important than those in the ribs, the sternum and the vertebral column. Most probably the condition is to be ascribed to pluriglandular insufficiency combined with poor nutrition. Improved dietaries and injections of 0.1 to 0.5 mg. of adrenalin resulted in improvement.—J. K.

(ADRENIN) Precipitation of epileptic attacks by adrenal extract (Über die Auslösung von epileptischen Anfällen mit Nebennierenextrakt). Benedek (L.), Wiener klin. Wchnschr., 1918, **31**, 1365.

Adrenin was injected in 19 patients subject to epilepsy. In seven cases this resulted in typical seizures. In other diseases and in normal individuals no similar reaction has ever been observed.—J. K.

(ADRENIN) The prophylaxis of hay fever. Lane (H. C.), N. Y. Med. J. (N. Y.), 1918, **108**, 859.

Adrenalin and the various pollen extracts and antigens give some relief and in many cases apparently relieve the pa-

tient for years, but, as a rule, eventually the hay fever recurs.
H. W.

(ADRENIN) The treatment of influenza with adrenalin (Die Behandlung der Grippe mit Adrenalininhalationen). Wolff-Eisner (A.), Münch. med. Wchnschr., 1919, **66,** 15.

Especially to prevent the occurrence of pneumonia, but also for the treatment of pneumonia as seen in the epidemic of influenza the author recommends the inhalation of adrenalin. He uses a spray and gives 4-6 inhalations a day. He saw only few complications with bronchopneumonia and even cure of some cases of severe bronchopneumonia.—J. K.

(ADRENIN) The use of adrenalin in malaria (Über die Anwendung des Adrenalins bei Malaria). Abl (R.), Münch. med. Wchnschr., 1919, **66,** 180.

The injection of 1 mgr. adrenalin causes a contraction of the spleen. The latent parasites appear in the blood. After the treatment of malaria by quinin it is necessary to examine the blood following an injection of adrenalin to see whether there are still latent parasites in the body.—J. K.

(ADRENIN) Tyrosinase in human urine (Über die Ausscheidung von Tyrosinasen in menschlichen Harn). Gross (O.), Deutsche med. Wchnschr. (Berl.), 1919, **45,** 488.

The author found in urine of a patient with a melanosarcoma of the liver, tyrosinase. This enzyme may transform adrenaline into a brown substance of unknown chemical properties.—J. K.

ASTHMA considered in its relationship to the vegetative nervous system. Pottenger (F. M.), N. Am. Clim. & Clin. Assn. (Phila.), 1917, **33,** 129-41.

Published elsewhere. See Endocrin. **2,** 317.

(AUTONOMIC N. S.) So-called irritable heart of soldiers. Lyter (J. C.), Proc. Mo. State M. Assn., J. Am. M. Assn. (Chgo.), 1919, **72,** 1937.

After studying the subject in the military camp at Camp Custer, Mich., Lyter is convinced that this syndrome, which was first described by Da Costa during the Civil War and by the French, English and American physicians during the recent war, is not a cardiovascular disturbance primarily, but the disturbance of the autonomic and sympathetic nervous sys-

tem. This syndrome occurs most often in the "hypoplastic" class of patients. The syndrome is a nervous disturbance most probably having its origin in a psychic disturbance resulting from a conflict of desires. The hypoplastic individual, having an unstable nervous system, manifests the symptoms more pronouncedly than other classes of individuals.—Official Abst.

(BLOOD SUGAR, ADRENIN) The influence of intravenous injection of Witte's peptone upon the sugar content of the blood and epinephrine hyperglycemia and glycosuria. Kuriyama (S.), J. Biol. Chem. (N. Y.), 1917, **29**, 127-139.

The blood sugar content of rabbits shows a tendency to increase after intravenous injections of Witte's peptone in doses of 0.5 to 0.75 gms. per kilo of body weight, the hyperglycemia lasting for a few hours only. No differences were observed when using boiled or unboiled peptones. The intravenous injection of gelatin or egg albumin has little or no influence upon the sugar content of the blood. Although an intravenous injection of peptone may be without marked influence upon epinephrin hyperglycemia, glycosuria is distinctly diminished. The same result is obtained with gelatine and egg albumin.—F. S. H.

CHOROID PLEXUS, Artificial stimulation of the—and experimental poliomyelitis. Flexner (S.), Amoss (H. L.) and Eberson (F.), J. Exp. Med. (N. Y.), 1918, **27**, 679-87.

Dixon and Halliburton have reported that intravenous injections of extracts of choroid plexus cause an augmented secretion of cerebro-spinal fluid. This observation is confirmed both in dogs and monkeys.—H. W.

CORPUS LUTEUM. Hirst (J. C.), Trans. Obst. Soc. of Philadelphia. Am. J. Obst. (York, Pa.), 1919, **79**, 495.

"I have found it essential to give corpus luteum by deep intramuscular injections, and not subcutaneously or by mouth. By the subcutaneous method there has been little effect; by the mouth, none whatever."—H. W.

CORPUS LUTEUM extracts, A biological test for—in vitro. Macht (D. I.) and Matsumoto (S.) Proc. Soc. Exp. Biol. & Med. (N. Y.), 1919, **16**, 86-87.

Aqueous, saline extracts of fresh or desiccated corpus luteum were found to exert a powerfully stimulating effect on

the vas deferens and seminal vesicles. Only adrenal and orchitic extracts have a comparably marked action. The vasa deferentia of the dog, cat, rabbits, guinea pig and rat were all found to react similarly, but that of the rat is most sensitive. Contractions occur with extracts as dilute in some cases as 1:2500, and nearly always with 1:1000. Though very sensitive to corpus luteum, the vas does not react to ovarian substance proper. The activity of corpus luteum preparations as indicated by vas deferens preparations runs parallel to that indicated by other clinical and experimental tests. This tissue is recommended, therefore, for the physiological assaying of corpus luteum preparations.—R. G. H.

(CORPUS LUTEUM) Sur les rôles du Corps Jaune. (Role of corpus luteum). Mulon (C.) Ann. de Gynec. et d'Obstet. (Paris), 1916-1917, 2me. Series, **12,** 545.

Continuation of a discussion of the part played by the corpus luteum in the production of hydatid-mole, extrauterine pregnancy, abortion, growth and secretory function of the mammary gland, arterial pressure, calcium elimination, gaseous exchange, adiposity, chlorosis, eclampsia, and the interglandular reaction. To be continued.—F. S. H.

(CORPUS LUTEUM) The control of the nausea and vomiting of pregnancy by intramuscular injections of corpus luteum extract. A report of the final results in one hundred and eleven consecutive cases. Hirst (J. C.), Am. J. Obst. (York, Pa.), 1919, **79,** 327-32.

Of 111 cases of nausea and vomiting due to pregnancy, 65 were entirely relieved, and 34 improved to the point where further administration of corpus luteum extracts was discontinued. Thus 99 of the 111 patients were entirely relieved or made comfortable. In 8 cases no beneficial results were obtained; in 4 nausea was increased. These 4 cases demonstrated large goiters. Hence, 12 were not improved and 4 made worse. Two cases gave anaphylactic reactions. Four of the cases aborted. In 11 cases classed as pernicious, 6 were completely relieved; 5 failed to respond to the treatment; in 2 cases pregnancy was interrupted to control the nausea and vomiting. Hirst uses ampules containing ⅓ grain of the soluble corpus luteum powder in 16 minims of physiologic salt solution saturated with chlorbutanol for its local anesthetic effect. This amount is equal to 2½ grains of the desiccated corpora lutea. All preparations, cow, sheep or pig, have about the same potency. A series of 12 ampules injected intramuscularly should constitute the treatment in these cases. One or

two ampules a day may be necessary at times to control vomiting. —H. W.

CORPUS LUTEUM, The use of—in the treatment of the nausea and vomiting of pregnancy. Cummins (E. J.), Southwest. Med. (El Paso.), 1917, **1**, 38.

In five out of six cases the intramuscular injection of corpus luteum extract relieved the nausea and vomiting of pregnancy and no untoward effects were observed.—F. S. H.

(CORPUS LUTEUM) The relation of the corpus luteum to menstruation (Über die Beziehungen des Corpus Luteum zur Menstruation). Seitz (L.) and Wintz (H.), Monatschr. f. Geburtsh. u. Gynäk. (Berlin), 1919, **1**, 49.

In a series of 177 ovariotomies presenting serous or pseudomucinous cystomas, parovarian cystomas, dermoids, or complicated by peritonitis, and where both unilateral and bilateral excisions were necessary, it was observed that the operative procedure was followed by discharge of blood from the uterus in but three cases. This evidence leads the authors to the conclusion that uterine hemorrhage, insofar as it is of menstrual type and cannot be attributed to other causes, is connected with the functional condition of the ovaries. Observations made at the time of occurrence of menstrual flow after operation in which the corpus luteum was removed, one series made during the first half of the intermenstrual period, and a second series during the last half, brought out that the flow occurred usually within three days after the operations when this took place in the last half, and was delayed three weeks or more when the surgical procedure occurred during the first half of the intermenstrual period. As a result of these and other observations the following conclusions were drawn. I. Histological, biochemical, and experimental investigations, as well as results obtained in X-ray castration, show that the menstrual cycle can be differentiated into and allocated to various phases of function of the ovary, as well as to changes in the endometrium. II. The phases of the ovarian cycle are as follows: 1. Ripening of the follicles. (Lipamin gland.) 2. Corpus proliferativum, the hitherto unobserved intermediary stage between ripened follicles and ripened corpus luteum. 3. The hyperemic stage of the corpus luteum. 4. The regressive stage of the corpus luteum. III. The ripening follicle brings about the premenstrual change of the mucosa and perhaps also the proliferative phase of the endometrial cycle. The corpus proliferativum of the corpus luteum brings the pre-

menstrual condition to full development and brings about the secretory phase of the endometrium. Both ripening follicles and corpus proliferativum prepare with increasing intensity the fore-conditions of menstrual flow. The hyperemic phase of the corpus luteum underlies the secretion phase of the endometrium and inhibits by its hormone the onset of menstruation. When the corpus luteum goes into the regressive phase the inhibiting influence of its hormone declines and the menstrual flow begins.—F. S. H.

CORPUS LUTEUM, The significance of the—. Epley (C. O.), J. Iowa State M. Soc. (Des Moines), 1917, **7**, 215-218.

As a result of studying the literature and the favorable outcome from feeding three cases having menstrual disorders with 5 grains of desiccated corpus luteum, the author considers that whenever it can be demonstrated that the patient lacks the internal secretions from the ovary, corpus luteum medication in some form is indicated. The specific indications for its use are: Profuse menstruation at puberty; disturbed artificial or normal menopause; amenorrhea and sometimes dysmenorrhea; nausea of pregnancy; nervous symptoms of pregnancy; infantile uterus; threatened abortion. The probable indications are: Acne, eczema, prurigo, acne and chlorosis of puberty and osteomalacia.—F. S. H.

DIABETES, Acetone bodies in the blood in—. Fitz (R.) Tr. Assn. Am. Physicians (Phila.), 1917, **32**, 154-58.

By the Van Slyke method the total acetone bodies, acetone, diacetic acid and betahydroxybutyric acid, were determined and expressed as acetone. The degree of acidosis was determined by measuring the combining power of plasma for CO_2. A series of 100 cases was tabulated, giving simultaneous determination of total acetone in the blood plasma and degree of acidosis. Some of the cases had severe acidosis and others were acid free. No comatose cases or those having had alkali were included. No definite quantitative relationship was discovered between increased concentration of acetone and lowering of blood bicarbonate, but in a general way the acetone rose as bicarbonate fell. The total acetone was increased by large amounts of fat, the maximum occurring several hours after ingestion and after visible lipemia had disappeared. Small amounts of fat depressed blood acetone. Fasting and pure carbohydrate diet diminished high acetone. Sodium bicarbonate increased acetone output, but its effect on blood acetone was uncertain. In three fatal cases of coma it was observed that a rapid premortal rise of blood acetone occurred. In one case this was independent of acidosis.—R. G. H.

(DIABETES) Acidosis in relation to pancreatic diabetes. Jensen (V. W.), J. Biol. Chem. (N.Y.), 1918, **33,** viii.

In studying the effect on the production of glycosuria by introduction of acid into a dog previously rendered glycosuric by removal of six-sevenths of the pancreas, it was found that 600 cc. of 0.1 NHCl given in three lots of 200 cc. each, during twenty-four hours, doubled the sugar excretion, while the same treatment of a dog sensitized by removal of five-sixths of the pancreas did not produce glycosuria. This indicates that acidosis is a result of the glycosuric condition and after it has developed it acts as part of a vicious circle.—F. S. H.

(DIABETES) Action of chloroform. Aloi (V.), Riforma med. (Naples), 1918, **34,** 890.

Results are reported which appear to confirm the increased excretion of urea, ammonia and total nitrogen after chloroform anesthesia. Diabetes induces lesions analogous to those of chloroform. The author was able to determine directly the presence of B-hydroxybutyric acid in 9 of 11 cases as the immediate result of the inhalation of chloroform.—Physiol. Abst., **4,** 143.

(DIABETES, BLOOD SUGAR) De bloedsuiker in de tropen. de Langen (C. D.) and Schut (H.) Geneesk. Tijdsch. ned. Indië, 1916, **56,** 490-551.

The blood sugar is 30 to 75 per cent higher in the tropics than in Europe; this is independent of race. This must affect the metabolism and may account for the frequency of diabetes and neuritis in the tropics.—Physiol. Abst., **4,** 17.

BLOOD SUGAR, Clinical significance of—in nephritis and other diseases (First paper). Williams (J. R.) and Humphreys (E. M.) Arch. Int. Med. (Chgo.), 1919, **23,** 537.

The average blood sugar level as determined upon a series of 113 normal individuals was 0.107 per cent, the values ranging from 0.07 to 0.14 per cent. In a series of 60 cases of miscellaneous diseases, gastro-intestinal and pernicious anemia, the average of the blood sugar level was 0.115 per cent, ranging from 0.07 to 0.16 per cent. In 9 cases of carcinoma there was a moderate elevation of blood sugar, 0.12 to 0.16 per cent. In 22 miscellaneous infections the values ranged from 0.07 to 0.15 per cent. with an average of 0.11 per cent. During the early stages of nephritis, when the general metabolism is but little disturbed, blood sugar, as a rule, is normal. In the last stages

of nephritis, when the patient is uremic, the blood sugar is found high, often equalling the severe stage of diabetes. Cardiovascular cases, characterized by high blood pressure and little or no evidence of renal disturbance, usually exhibit blood sugar levels higher than normal. Patients may excrete small quantities of sugar in the urine. In such cases the blood sugar level is inappreciably influenced by carbohydrate restriction. Failure in nitrogen metabolism precedes, often by months, the rise in blood sugar.—H. W.

(DIABETES) The clinical significance of blood sugar in diabetes mellitus (Second paper). Williams (J. R.) and Humphreys (E. M.) Arch. Int. Med. (Chgo.), 1919, **23**, 546.

The renal threshold should be considered the height of the blood sugar level at which appreciable quantities of sugar are eliminated in the urine. The blood sugar level in various stages of diabetes may be much higher or lower than the renal threshold. No striking relation is found to exist between the height of the renal threshold and the duration of the diabetes. Young diabetics, as a rule, show a low or normal threshold. The threshold appears to rise with advancing years. When the diabetes is mild or quiescent, the point at which the kidneys eliminate sugar is stationary; but when the disease becomes progressive, the threshold tends to rise. Before death the blood sugar renal threshold may reach great heights with little or no sugar appearing in the urine. A high renal threshold for sugar in mild diabetes under proper dietary regulations usually indicates some complication, as arterial hypertension. A high renal threshold for sugar may mean a physiological expedient to conserve food material. A high, persistent blood sugar level promotes exhaustion and rapid decline of function, hence, the higher threshold is simply a safety measure. In severe diabetes, when extremely low diets are necessary to maintian life, the high threshold is essential to compensate for the impaired carbohydrate metabolism. In the treatment of diabetes it is desirable to maintain the blood sugar level as nearly normal as possible, even though severe restrictions in diet may be necessary for this purpose, notwithstanding the fact that the high threshold will permit of a much more liberal diet without the appearance of sugar in the urine. Patients are apparently safer when the maximal digestion blood sugar level is not higher than 0.13.—H. W.

(DIABETES) Observations on tolerance and rate of utilization of glucose in a series of individuals exhibiting various degrees of diabetes mellitus. (Third paper). Williams (J. R.),

and Humphreys (E. M.) Arch. Int. Med. (Chgo.), 1919, **23**, 559.

The authors highly recommend the Janney modification of the Hamman and Heischman method as a means of measuring the degree of disturbance in carbohydrate metabolism in hyperthyroidism and other endocrinal disorders, this being much superior to tests depending wholly on the determination of urine sugar. Renal diabetes is considered a definite physiological disturbance, easily distinguished by the above mentioned process from true diabetes. A number of reports and protocols are included.—H. W.

(DIABETES) Clinical Calorimetry. Twenty-fourth paper. Metabolism in three unusual cases of diabetes. Gephart (F. C.), Aub (J. C.), Du Bois (E. F.), and Lusk (G.), Arch. Int. Med. (Chgo.), 1917, **19**, 908-930.

A paper dealing with the measurement of the respiratory exchange and total heat production of three diabetics undergoing the starvation treatment. It was observed that metabolism was markedly decreased in all cases and in one some 40 per cent below the normal for the age and weight of the individual studied. With the increase in sugar tolerance there was a synchronous rise in metabolic level.—F. S. H.

DIABETES, Dietetic helps in—. Donk (Rose R.), J. Am. M. Assn. (Chgo.), 1919, **73**, 25-27.

It is with difficulty that the busy practitioner finds time to carry out the exact regulation of diet that the proper treatment of diabetes demands. The dietary requirement depends upon the age, weight, condition as regards obesity and habits of exercise. Acidosis must be prevented. The metabolic derangement of diabetes involves protein and fat as well as carbohydrate metabolism, hence the beneficial effect of "fast days." Carbohydrate tolerance is relative as shown by improvement when protein is kept at a sufficiently low level. Accurate laboratory control is essential. Although the blood urea is low the patient commonly has a high urinary urea output. Like the hyperthyroid or fever patient the diabetic overexcretes and overconcentrates. If in becoming sugar-free and acid-free the patient lowers a high urea index he has scored an extra point. Fat ingestion should be regulated by determinations of acetone bodies, acid and ammonia of the urine. Alveolar air determinations are a reliable guide as regards acidosis. The Marriott apparatus is simple and sufficiently accurate.

A case is reported with full laboratory details of a fairly severe diabetes in which the patient ultimately regained an ability to utilize 83 gms. protein, 147, fat and 58, carbohydrate, giving 1887 calories. In order to eliminate as much as possible of the drudgery of regulating the gradual dietary progress of the patient in accordance with the laboratory findings, an elaborate set of tables is given. Starting with fixed quantities of 5 per cent. vegetables, from 200 to 5000 gms., the effect is given of adding various quantities of potato, bread, broth, fish, egg, cream, butter, lean meat, cheese, bacon and olive oil. This, in effect, gives a progressive chart of augmenting protein, fat, carbohydrate and caloric values the exact degree of which is indicated without laborious calculations. The total range is from 40 to 1778 calories.—R. G. H.

(DIABETES) Diffuse diabetic ulceration of the pharynx and larynx. Arrowsmith (H.), Laryngoscope (St. Louis), 1916, **26,** 1177-78.

Report of a case of diabetic ulceration of the uvula, velum and posterior pharyngeal wall, the laryngeal surface of the epiglottis and right arytenoid of 5 months standing in a woman 66 years old. The Wassermann test was negative; there were no tuberculous findings. The Allen treatment brought about a marked improvement of her glucemia, but the local condition remained unaltered.—H. W.

DIABETES, Edema as a danger signal in the starvation treatment of. Croftan (A. C.), J. Am. Med. Assn. (Chgo.), 1917, **69,** 1962-1963.

The benefit to be derived from the starvation treatment of diabetes is exaggerated since no increased sugar tolerance was found and since there was a marked increase in acetone bodies accompanied by edema. These conditions disappeared when small amounts of carbohdyrate food were ingested. A diuresis followed, but was not accompanied by compensatory glycosuria. This phenomenon is due to the fact that in hunger the urine output is low and water retention by the tissues causes the appearance of the edema, which is a danger signal. This can be prevented by the use of pancreatized oatmeal-alcohol-glycerin clysmata.—F. S. H.

(DIABETES) Glycosuria complicated with maltosuria and dextrinuria (Glycosurie compliquée de Maltosurie et de dex-

trinurie). Gaillard and Fabre, J. Pharm. et Chim. (Paris), 1917, **7,** 129-137.

A case of traumatic diabetes arising from concussion syncope followed by vertigo, instability, etc. Analysis of the urine showed the presence of 25-26 gms. glucose, 36-37 gms. dextrine and 35-36 gms. maltose per litre. This is attributed to involvement of the central nervous system—F. S. H.

DIABETES in children. Gray (H.) and Joslin (E. P.) Tr. Assn. Am. Physicians (Phila.), 1917, **32,** 149-54.

Among the private cases of diabetes of the authors 4.7 per cent fall within the first decade of life, a proportion materially higher than in well known earlier statistics. The same etiologic factors are found as in adults, but obesity, dietary excesses, heredity and mental over-exertion are most commonly observed. Fatness of undue degree in children is very prone to be followed in later life by diabetes. A child with hereditary history of diabetes has, in the authors' experience, a more favorable outlook than one free from hereditary taint. Low blood sugar in children is not ground for undue complacency. Repeatedly children of low sugar type have developed progressive diabetes. Children make exceptionally good patients, responding well to proper dietary therepeusis and, as a rule, complaining little. Growth often takes place normally—a fact that is likely to lead to a false conclusion that a cure has been effected. The treatment is precisely the same as in adults, namely, rigorous restriction of eating. Complete fasts are usually well borne. Following the fast, administration of 50 grams of 5 per cent vegetables with broths is effective in relieving hunger, and subsequent weekly strict diet days cause no trouble if broths and 300 grams of 5 per cent vegetables can be allowed. Special pains should be taken in the preparation of the vegetables, for children eat rapidly and diarrhea occasionally results. Constipation, however, is more common. The diet should not be made too simple.—R. G. H.

DIABETES insipidus. Barach (J.H.), Am. J. Med. Sc. (Phila.), 1917, **154,** 220-225.

A case of diabetes insipidus with kidneys capable of eliminating a normal amount of solids in twenty-four hours. In response to ingestion of added amounts of salt or urea the elimination was prompt and rapid. The ingestion of 100 gms. of glucose was followed by a slight transitory glycosuria and diuresis.—F. S. H.

DIABETES INSIPIDUS due to hemorrhage into the neurohypophysis (Diabete insipido da enorragia nella neuroipofisi). Luzzato, Riforma med. (Napoli), 1918, **34**, 94.

See Endocrin., 1918, **2**, 32.

(DIABETES) La chirurgie chez les diabétiques (Surgery in diabetics). Labbé (M.), Ann. de méd. (Paris), 1918, **5**, 428. Abst. Surg. Gyn. & Obst. (Chgo.), 1918, **28**, 407-8.

The danger of operating upon diabetics arises principally from hyperglycemia which favors suppuration, and acidosis leading to post-operative coma. Only absolutely necessary operations should be undertaken. When not urgent the operation should be preceded by a diabetic regimen. Immediately before operation fasting should be suspended and 40 gms. sodium bicarbonate given. Local anesthesia with cocaine or one of its congeners should be utilized if possible, with spinal anesthesia as second choice. If general anesthesia is imperative ethyl chloride should be used. No diabetic patient should be subjected to ether or chloroform. After operation sufficient sodium bicarbonate—up to 100 grams—should be given to produce an alkaline urine. When the patient is able to eat, vegetable broths, oats, dry vegetables and milk should be given, with continuation of the alkaline treatment until acidosis has disappeared.—R. G. H.

DIABETES mellitus, A case of—, with apparent recovery. Colquhoun. New Zealand Med. J. (Wellington), 1917, **16**, 5-7.

On a regular diabetic diet an individual previously showing a daily glucose elimination of 32.8 grams decreased the sugar output to 26.3 grams during a month's treatment. A high protein diet following resulted in a decrease of the sugar output to zero within two weeks. The later admission of carbohydrates to the diet did not produce a recurrence of the glycosuria.—F. S. H.

DIABETES mellitus, Psychoses associated with. Singer (H. D.) and Clark (S. N.), J. Nerv. & Ment. Dis. (N. Y.), 1917, **46**, 421-428.

Toxic hallucinoses often coincide with the diminution of sugar elimination, though not according to any rule and without any apparent explanation. Two cases are reported. With the reappearance of the sugar the hallucinations disappeared. —F. S. H.

DIABETES mellitus, Recent studies in—. Williams (J. R.), N. Y. State M. J. (N. Y.), 1916, **16,** 412-18.

Young patients do well on the Allen treatment. Diabetes is more amenable to treatment when not complicated with infection or arterial degeneration. Syphilis is probably a rare factor in the causation of diabetes. Of the 10 patients who died (82 cases observed), 4 succumbed to exhaustion occasioned by severe surgical operations; none of them died in coma. The others would not follow the treatment. Advanced cases should not be subjected to starvation methods too rapidly as fatal results have followed such procedures.—H. W.

DIABETES mellitus, The Allen-Joslin treatment of—. Woldert (A.), N. Y. Med. J. (N. Y.), 1918, **108,** 764-7.

A general statement of the methods used in the treatment of diabetes mellitus.—H. W.

DIABETES MELLITUS, The maintenance diet in—as determined by the nitrogen equilibrium. Mosenthal (H. O.) Tr. Assn. Am. Physicians (Phila.), 1917, **32,** 159-71.

Metabolic studies on nine diabetics are reported. It was found that patients could be established in nitrogen balance by a protein-fat diet having a caloric value equal to the standard caloric requirement. In many cases nitrogen equilibrium is possible at a sub-standard caloric level. The factors determining the minimal level at which balance can be maintained are apparently very numerous and partially unknown, but glycosuria and slight infections are two that may necessitate an increased food intake to avoid a nitrogen deficit. It is necessary to maintain nitrogen equilibrium if the physical and mental efficiency of the patient are to be conserved. On a carbohydrate-free regime this amounts roughly to 1500-2000 calories, women and smaller individuals in general requiring less than normal size men. A positive nitrogen balance may be attained in diabetics while on carbohydrate-free diet.—R. G. H.

DIABETES, Observations on the starvation treatment of— Martin (C. F.) and Mason (E. H.), Tr. Assn. Am. Physicians (Phila.), 1916, **31,** 444-54.

Published elsewhere. Abst. Endocrin., **1,** 529.

DIABETES, On sudden changes of refraction in—. Zimmerman (C.), Wisconsin M. J. (Milwaukee), 1915-1916, **14,** 227-31.

Report of a case of sudden development of myopia in a diabetic man 52 years of age. Treatment of the diabetes

brought about marked improvement of vision. The various theories concerning the etiology of refractive changes in diabetes are thoroughly discussed.—H. W.

DIABETES. On xanthosis diabetica (Über die Genese der Xanthosis diabetica.) Bürger (H.) and Reinhart (A.) Deutsche med. Wchnschr. (Berlin), 1919, **45**, 430.

The so-called xanthosis diabetica has nothing to do with diabetes. It may be seen in all patients and is normal in persons when they are fed during a long time only on green vegetables.—J. K.

(DIABETES) Pancreatic diabetes in the dog. I. The influence of alkali and acid upon the glycosuria and hyperglycemia. Murlin (J. R.) and Kramer (B.) J. Biol. Chem. (N. Y.), 1916, **27**, 481-498.

Sodium bicarbonate and potassium bicarbonate administered by stomach tube may be without immediate effect on the glycosuria and hyperglycemia of the depancreatized dog. A bicarbonate given by mouth to a fasting depancreatized dog may even cause the reappearance of glucose in the urine after it has been "starved" out. The normal anhydrous sodium carbonate may, on the contrary, reduce the sugar in the urine materially when given by mouth, and when given by vein invariably does so, especially when added to Ringer's solution to the amount of about 1%. The blood sugar does not undergo a compensating increase in percentage even when the dilution of the blood is accounted for. Dilute HCl given by mouth or subcutaneously to the depancreatized dog has just the opposite effect of alkali, increasing the sugar in the urine without materially affecting the nitrogen elimination, and without causing any effect on the blood.—F. S. H.

(DIABETES) Pancreatic diabetes in the dog. II. Is the glucose retained when sodium carbonate is administered to depancreatized dogs deposited as glycogen? Kramer (B.), Marker (J.) and Murlin (J. R.) J. Biol. Chem. (N. Y.), 1916, **27**, 499-515; Proc. Am. Soc. Biol. Chem., 1916, xxiv.

Neither the direct determination of glycogen in liver and muscle of depancreatized dogs to which had been given sodium carbonate with consequent diminution of glycosuria, nor the feeding of glycogenetic material plus sodium carbonate to deglycogenized dogs with study of the subsequent degree of glycosuria under further deglycogenization, succeed in producing

evidence that the glucose retained is held back as glycogen.
—F. S. H.

(DIABETES) Pancreatic diabetes in the dog. III. The influence of alkali on the respiratory metabolism after total and partial pancreatectomy. Murlin (J. R.) and Kramer (B.) J. Biol. Chem. (N. Y.), 1916, **27**, 517-537.

In completely depancreatized dogs the administration of sodium carbonate by mouth or intravenously is promptly followed by a retention of considerable amounts of glucose of endogenous or exogenous origin. In partially depancreatized dogs which still have some capacity to oxidize glucose, the administration of sodium carbonate or sodium hydroxide with glucose is followed by a greater oxidation of glucose than when either is given alone. Sodium carbonate itself causes but a slight increase in respiratory quotient, or none, whether administered per os or intravenously, to normal or diabetic dogs. The retention is rarely if ever accompanied by any evidence of improved oxidation. Thus, while it seems that sodium carbonate or sodium hydroxide alone cannot restore the lost function to an organism completely deprived of its ability to oxidize glucose, either substance can improve the capacity of the organism as a whole to oxidize glucose when this function is more or less crippled but not completely lost.—F. S. H.

DIABETES, Salt metabolism in—. Beard (A. H.) and Rowntree (L. G.) J. Biol. Chem. (Balt.) 1918, **33**, xx. See also Arch. Int. Med. (Chgo.), 1918, **21**, 716-739, Abst. Endocrin. **2**, 320.

If diabetic patients are followed to ingest salt ad libitum they consume very large amounts and in many cases the gain in weight and the development of edema is synchronous with, and in all likelihood dependent upon, retention of salt and water.—F. S. H.

(DIABETES) Studies of acidosis. IV. The blood, urine, and alveolar air in diabetic acidosis. Stillman (E.), Van Slyke (D. D.), Cullen (G.), and Fitz (R.), J. Biol. Chem. (Balt.), 1917, **30**, 405-456.

The alveolar air carbon dioxide tension in diabetic patients under treatment is often much too low to indicate the true level of the blood bicarbonate. In very severe acidosis the urine index is less accurate than the alveolar air in indicating the alkaline reserve. Of the two indirect measures of alkaline reserve, therefore, the alveolar carbon dioxide appears to be

the more accurate in measuring the more severe stages of diabetic acidosis, such as are encountered in threatened coma, while the index of acid excretion is more accurate in the more common intermediate stages.—F. S. H.

DIABETES, The Allen treatment of—. Friedenwald (J.) and Leinbaugh (L.) Interstate M. J. (St. Louis), 1916, **23**, 71-79.

Report of 20 cases of diabetes treated by the Allen method. All were rendered sugar free in from one to four days, and, save for one case which would not follow the dietary measures, kept free from sugar. In a very few instances in which sugar reappeared, the condition was overcome by a single day's fast.—H. W.

(DIABETES) The concentration of dextrose in the tissues of normal and diabetic animals. Palmer (W. W.), J. Biol. Chem. (Balt.), 1917, **30**, 79-114.

The concentration of dextrose was determined in muscle, liver, heart, kidney, spleen, pancreas, stomach, intestine, skin, lung, and eye tissues of normal and diabetic animals, under varying conditions of procedure. No difference in the amount of dextrose to be found in either normal or diabetic tissues is caused by variation in the manner of producing the hyperglycemia. The concentration of dextrose varies directly with the degree of hyperglycemia. The largest amount of sugar was found in the liver, the smallest in the brain, the difference being accounted for by the difference in vascularity. The concentrations of dextrose in the tissues, with the exception of the liver, was invariably lower than that of the blood. Normal animals have a higher concentration of dextrose in striated muscle than have diabetic animals when the levels of blood sugar are comparable. Bleeding of an animal causes a rapid glycogenolysis in the liver. Adrenalin produces no change in tissue sugars different from that found when hyperglycemia is caused by other means.—F. S. H.

(DIABETES) The influence of renal function on hyperglycemia and glycosuria in diabetes mellitus. Epstein (A. A.), Am. J. Med. Sc. (Phila.), 1917, **154**, 103-121.

Clinical reports of cases of diabetes with and without nephritis comparing the blood and urinary sugar and also renal function using the phenolsulphonpthalein test. From these it is concluded that: 1. A condition simulating renal diabetes, i.e., a glycosuria without hyperglycemia, may occur in diabetes

mellitus. This is brought about by an increase in blood volume which reduces the concentration of the blood sugar, and the consequent fall in its percent masks the hyperglycemia. 2. Hyperglycemia without glycosuria is of frequent occurrence in diabetes mellitus. When sugar is absent from the urine a persistent hyperglycemia which remains constant or does not progress, shows an altered state of carbohydrate metabolism in which a balance is established between the supply of sugar to the blood and its ultilization by the tissues on a higher plane than that found normally. This is interpreted as an increased tolerance of the kidneys. A true nephritis need not interfere with the elimination of the sugar. Testing the kidney function by means of phenolsulphonpthalein in diabetes mellitus is a useful procedure. It aids in understanding the relation of the hyperglycemia to the glycosuria. It is particularly helpful in those cases in which a fall in the urinary sugar is associated with a rise in blood sugar, thus yielding confirmatory evidence of the fact that the elimination of glucose is interfered with.—F. S. H.

DIABETES, The role of fat in—. Allen (F. M.), Am. J. Med. Sc. (Phila.), 1917, **153**, 313-371; see also N. Y. Med. J. (N.Y.), 1916, **104**, 1005.

In studies on partially depancreatized dogs it was observed that a lipemia could be developed by regulating the diet. The visible blood fat in the lipemic dogs was not in an abnormal form insoluble in ether. The power of the plasma to hold the fat in clear solution was not diminished, and there was a low total fat content of the corpuscles. The condition was due neither to a hyperglycemia, an absence of carbohydrates, nor to a loss of sugar from the body. It was not due to the presence of acetone bodies, nor to the change in reaction of the blood. It was not due solely to the partial removal of the pancreas. Nor was it due to a breaking down of a hypothetical "fat function" by direct overstrain of that function. It does depend, however, upon the severity of the diabetes, hence the disorder underlying the lipemia is bound up to a considerable extent with the other diabetic disturbances and is not entirely independent, its exact focus being at present undetermined. The production of an acidosis in partially depanereatized dogs on a high fat diet can lead to coma with a terminal low carbon dioxide capacity of the plasma, which can be relieved by bicarbonate treatment but which does not prevent the death of dogs dying of acidosis. Increased ammonia excretion and the elimination of acetone bodies also occur. The addition of fat to the diet caused a distinct depression of blood sugar. An attempt

at high nutrition with fat produces a spontaneous aggravation of the condition. Accordingly the experiences with diabetic dogs warns unmistakably against efforts to maintain patients on a luxus level of diet or weight, and the standard of feeding should approximate that of Chittenden rather than that of Voit.—F. S. H.

(DIABETES) The present outlook of diabetic treatment. Allen (F. M.), Tr. Assn. Am. Physicians (Phila.), 1917, **32**, 139-48; Med. Rec. (N. Y.), 1917, **92**, 39.

Three years after the Allen treatment was first instituted, the originator of it sums up accomplishments and future outlook. It appears that the most accurate standard of severity of the disease is not acuteness of onset, rapidity of progress, intensity of glycosuria or degree of acidosis. The genuinely difficult cases are those in which the sugar tolerance is practically nil and fails to increase under prolonged, rigorous treatment.

In experimental diabetes in animals specific degeneration of the islands of Langerhans occurs; this is characterized by vacuolation of cytoplasm, pyknosis of nuclei, loss of cells and finally almost complete disappearance of the islands. Partial pancreatectomy does not produce diabetes in animals if these are fed within their tolerance, but overtaxing this tolerance will at any time initiate the degenerative changes in the islands. The clinical progress of the resulting diabetes and the degree of exhaustion and degeneration of the cells run parallel. When extreme exhaustion is reached death is inevitable. Although excellent pathologists have failed to find similar exhaustion and denegeration in the Langerhans cells of some cases of human diabetes, such have been found in all fatal cases at the Rockefeller Institute Hospital. It is emphasized, however, that the tissues for microscopic diagnosis should be secured immediately after death.

Allen feels that the death of any patient in which structural defects of the pancreas can not be demonstrated lays the treatment administered under grave suspicion, it being probable that proper conservation of tolerance would have saved the patient. The worst form of treatment is that which permits death from coma or similar avoidable accident. The next worst is that which slowly destroys the Langerhans cells by continuously overtaxing them. The only present hope for diabetics is treatment by functional rest, with conservation of what viable Langerhans cells remain and, possibly, regeneration of others.—R. G. H.

DIABETES, The starvation treatment of—. Marshall (M.), J. Mich. State M. Soc. (Grand Rapids), 1916, **15,** 150-1; Tr. Clin. Soc. Univ. Mich. (Ann Arbor), **7,** 48.

M. obtained good results in the treatment of diabetes by the Allen method. Most cases so treated became sugar free in about three days.—H. W.

ENDOCRINE GLANDS and bone dystrophies. Editorial. N. Y. Med. J., 1919, **109,** 907.

Whether the subject presents hereditary syphilis, an infection or chronic intoxication, nervous stigmata or circulatory disturbances resulting from improper feeding, one will invariably find indices of a local or general pertubation of the nutrition. Frequently this is due to changes or functional disturbances arising in some set of endocrine glands which are the great regulators of metabolic changes. In the majority of cases the osseous dystrophies are due, not to a single given endocrine gland, but to several, so that they belong to a true pluriglandular syndrome.—H. W.

ENDOCRINE GLANDS and their relation to vaso-motor disturbances of the air passages, hay fever and asthma, with the past year's report. Selfridge (G.), Calif. State J. Med. (San Francisco), 1919, **17,** 139.

Among 26 cases of vaso-motor rhinitis 14 were found with signs of slight endocrine gland insufficiency. Signs of more or less marked endocrine disturbances were also noted in 22 cases of bronchial asthma; in 6 thyroid disturbances predominated, 15 demonstrated hypo-pituitarism, and one probably status lymphaticus. Observations upon eight cases demonstrated a striking relationship of anaphylaxis to pituitary disturbances. This relationship was present in those reacting to hairs, foods, bacteria and to colds which seemed to be anaphylactic rather than bacterial in origin. All of these cases showed abnormalities about the sella turcica. Chest radiographs of anaphylactic cases gave normal readings in contradistinction to the peribronchial thickenings commonly found in the class of so called "asthmatic bronchitis" or infective types. Endocrine therapy apparently relieved some of the cases of vaso-motor disturbances of the air passages, hay fever and asthma. However, time enough has not elapsed to warrant any definite statements or conclusions regarding such therapy.—H. W.

(ENDOCRINE GLANDS) On the use of internal glandular extracts in mentally retarded children. Timme (W.) Bull. Dep. Pub. Char. (N. Y.), 1916, **1**, 40-47.

The endocrine system comprises groups of glands that functionate during different epochs of life. In early years the pineal and thymus apparently control body growth and metabolism. These at puberty give way to the ovaries, testes and pituitary. After middle life one or the other of these latter becomes atrophied and a train of symptoms due to endocrine imbalance results. The thyroid and the adrenals act as regulators throughout life, controlling to an extent the others and compensating for them. The organ or tissue of the body that does not move harmoniously with the rest during early childhood becomes a drag upon its co-workers. Should the thymus, the pineal or the thyroid functionate abnormally, disturbance of growth occurs and the individual becomes backward mentally and bodily. If the pineal atrophies before puberty, precocity appears. If the pineal functionates beyond the normal age, a certain degree of infantilism results. The thymus that does not atrophy as the child advances in years, conditions a state of deficient evolution, especially of the connective tissues; the mentality is on a par with the physique, childish and backward. The thymus that ceases to act too early causes a precocious body growth; the muscles and bones, without apparent increase in size, give the appearance of age; the skeleton is abnormally brittle and subject to easy fractures. Three illustrative cases are described.—E. H.

(ENDOCRINE GLANDS) Phosphatides in the ductless glands. Fenger (F.), J. Biol. Chem. (Balt.), 1916, **27**, 303-307.

Chemical analysis of the amounts of phosphatides in the ductless glands of cattle show that the pituitary, the suprarenals, the pineal, the infant thymus, and the corpus luteum of pregnancy contain considerable amounts of phosphatides in excess of ordinary muscle tissue, indicating that the phosphatides play some part in the internal chemistry of the ductless glands. The thyroid does not contain any more phosphatides than lean meat, and it may, therefore, be assumed that this gland performs its secretory functions independent of the phosphatides.—F. S. H.

(ENDOCRINE GLANDS) The early recognition of some endocrinopathies. Timme (W.) Hosp. Bull. Dep. Pub. Char. (N. Y.), 1917, **1**, 33.

A few general principles should be kept in mind so that

the matter of recognition of the various signs and symptoms of internal glandular disorders be not reduced to a memory basis purely, but that associative aids in our interpretation be enlisted in our service. These general principles are, first, the activity of the pineal and thymus glands in infancy and childhood up to the period of puberty; they control constructive metabolism. At puberty the gonads come into the field; the pineal and thymus atrophy. The thyroid, pituitary and suprarenals are monitors over the others during life. The two series of glands being antagonistic, any invasion of the thymus or pineal in the domain of the gonads, or vice versa, results in changes in the individual as to growth, sexual development or mental precocity. Any change from the normal in any one gland must necessarily have compensating changes in the other glands. If sufficient compensation is lacking, we may have either under-compensation or over-compensation. The importance of interpreting the manifestations of a disturbed glandular system in terms of the proper gland originally at fault is evident. A synopsis is appended, giving the symptoms referable to the thyroid, suprarenal (cortex), suprarenal (medulla), pituitary, thymus and pineal glands.—E. H.

(ENDOCRINE GLANDS) Recovery of normal weight in the various organs of albino rats on refeeding after underfeeding from birth for various periods. Jackson (C. M.) and Stewart (C. A.) Am. J. Dis. Child. (Chgo.), 1919, **17**, 328.

The authors conducted experiments on albino rats, underfeeding the animals from birth to 3, 6 or 10 weeks of age and then refed them amply. The process of recovery on refeeding will vary according to the age at which the preceding inanition period began. This is evident if the results of the present experiments (beginning at birth) are compared with those published earlier by Stewart in 1918, in which the rats were amply refed after maintenance by underfeeding beginning at three weeks of age. In the rats in which the inanition tests began at the later date, most of the organs (excepting the testes, epididymi and suprarenals, which remained subnormal) had recovered approximately their normal relative weight within from two to four weeks of refeeding. The thymus and possibly the spleen and ovaries were apparently above normal (over-compensatory growth?) after from two to four weeks of refeeding. In the present experiments, the authors found different results. In general, inanition at the earlier age seems to have effected more permanent results, as reflected in the more tardy recovery of normal weight in several of the organs. The hypophysis and suprarenals are apparently nearly normal in weight in all groups. The testes, epididymi, brain, thymus, thyroid, and

ovaries show more or less retarded recovery in weight on refeeding. To this list may perhaps be added the pineal gland. This would seem to indicate that early inanition, especially when prolonged, tends to inhibit the later growth of the pineal gland. The testes and spleen show an apparent tendency to over-compensatory growth in the earlier stages of refeeding with later retardation. There is no evidence of over-compensatory growth in the thymus and ovaries. The results may perhaps indicate the probability of recovery in the various organs of infants after periods of inanition.—M. B. G.

ENDOCRINE ORGANS, Influence of the—on the physiological activity of the bladder (Die physiologishe Tätigkeit der Harnblase und ihre Beeinflüssung durch Produkte der inneren Sekretion). Abelin (J.), Ztschr. f. Biol. (Münch u. Berl.), 1919; **69,** 373.

Intravenous injections of adrenin diminish the contraction of the bladder. Pituitary extract causes a very marked increase of tonus; this is independent of its effects on blood pressure, vascular calibre or respiration. The bladder is, in fact, the best test object for assaying pituitary extract. It can be utilized in situ in the living animal, without anesthesia. Thyroid and thymus extracts have no effect on the bladder.—J. K.

(ENDOCRINE ORGANS) Juvenile endogenous adiposity. (Über endogene Festtsucht im späteren Kindesalter). Schucany (T.), Jahrbuch f. Kinderheilk. (Berlin), 1919, **69,** 30.

Two cases of adiposity in children, the first one caused by hypofunction of the thyroid, the second by a diminished function of the pituitary body. This latter case showed also eunuchoidism. The skeleton of the first patient was under-developed; the skeleton of the second showed a remarkable overgrowth. In both patients a good result was obtained by specific organotherapy.—J. K.

(ENDOCRINE ORGANS) Rare forms of pluriglandular insufficiency (Über seltene Formen der pluriglandulairen endokrinen Insufficienz mit Xanthosis, familiärem Ikterus, hypothyreogenem Oedem). Curschmann (H.) Ztschr. f. klin. Med. (Berl.), 1919, **87,** 19.

Three interesting cases are described. 1. A woman without diabetes had a classical xanthosis. Many symptoms of pluriglandular insufficiency were present, including genital atrophy and enormous hands and feet, but no changes in the

sella turcica. After her first pregnancy the symptoms increased rapidly; menstruation ceased and sex feelings disappeared totally. Organotherapy was not successful. 2. A boy at 12 developed glycosuria. At 19 he complained of stomach symptoms. No free HCl was found. He had jaundice, but no bile in the feces. Sexual functions ceased as did growth of hair and beard. 3. A man of 36 a year before his death developed edema of the legs, dry skin, typical pigmentation as in Addison's disease, testicular atrophy and sexual impotence. Fat appeared in the stools in large quantities. At autopsy the thyroid was found small and hard, but the pancreas and adrenals appeared normal.—J. K.

(ENDOCRINOLOGY) Evolucao da endocrinologia (Evolution of Endocrinology). Brazil (A.) Archivos de Biologia de San Paulo (Brazil), 1918, **3**, 439.

Brazil gives a long review to the more significant articles on Endocrinology. No new data are offered.—G. P. G.

(ENDOCRINOLOGY) The dominance of the endocrines. Garretson (V. P.) N. Y. Med. J., 1919, **109**, 839.

An understanding of the physiology relative to the endocrine and vegetative nervous systems is of paramount importance and proves an incalculable aid in the analysis and treatment of so-called functional derangements, as well as organic disease. The internal secretory glands are vegetative organs, and their function is to a degree regulated by the nervous system, while on the other hand the dominance of these glands over the nervous system is quite beyond dispute; especially is this evident as displayed through psychical or mental functions. In proof of this one has but to note the alterations in character that follow or are associated with disturbed endocrine function. The psyche is maintained in proper balance through the normal action of the vegetative nervous system. Its responses, in so-called psychic reactions, are dependent upon the endocrine functions. As a buffer to these vital functions, it responds in varying degrees as influenced by experiences based upon instincts and memory complexes, and the so-called shock reactions are accordingly expressed and reflected by symptomatic evidences. That large group of patients generally misunderstood and frequently classed in civil life as neurasthenics, psychasthenics, hysterics, cyclothymics, and hypochondriacs, is now capable of an intelligent analysis and rational therapy, if one will concede these are the victims of an endocrine asthenia. "The life of every individual is dominated by his ductless gland chain. Certain of the glands assume a dominating influ-

ence and by reason of this, we are able to designate persons in terms of glandular types. For example, studies clinically have proved that certain physiological and structural markings are constant to certain glandular types, and by the physical objective examination alone, without other information we can make an accurate diagnosis.''—H. W.

GOITRE from the standpoint of the internist. Anders (J.), Penn. Med. Jour. (Athens), 1917, **21,** 483-85.

A general clinical discussion of syndrome. Advocates the feeding of iodine for development in suspected cases.—F. S. H.

(GONADS) Development of heterosexual symptoms (Auftreten von heterosexulaen Merkmalen). Hermans (L.) Münch. med. Wchnschr., 1919, **66,** 157.

The author describes a case of a man of 38 years who, without known cause, developed atrophy of both testes. At the same time hypertrophy of the mammary glands appeared.
—J. K.

(GONADS) Evidence that the germ cells are subject to selection on the basis of their genetic potentialities. Danforth (C. H.), J. Exp. Zool. (Phila.), 1919, **28,** 385-413.

Not of endocrine interest.—M. M. H.

(GONADS) Interstitial cells in the gonads of the domestic fowl. Goodale (H. D.), Anat. Rec. (Phila.), 1919, **16,** 247-251.

The author believes that the granular interstitial cells of the ovary of the domestic fowl are eosinophile leucocytes. He has found cells like them among the erythrocytes in the blood vessels, in the active thymus of two moulting drakes, in the connective tissue of testes and epididymus, and rarely in the thyroid, pituitary and pineal glands. He calls attention to the presence in the ovary of a type of cell which is not demonstrably granular (called ''clear cells'' by some authors and ''luteal cells'' by Pearl and Boring). These he believes may be shown to be granular by the use of special stains, and may prove to be the true interstitial cells from the physiological standpoint.—M. M. H.

(GONADS) On the physiological properties of the gonads as controllers of somatic and psychical characteristics. Moore (C. R.), J. Exp. Zool. (Phila.), 1919, **28,** 137-161.

A study of the conditions following gonadectomy in young

rats and the subsequent transplantation of the opposite gonad to each animal (repetition of the experiments of E. Steinach) shows that the apparent effects of such a condition are not so marked as one is led to expect from Steinach's reports. Somatic changes that are due entirely to the presence of the implanted gland are difficult to demonstrate. From the psychical side the results are more definite. Young male animals have been converted into such apparent, typical females that the mother instinct to protect and nurse the young is readily noticeable. Also young females have been converted into such apparent, mature males that they react psychically as males and imitate a male, in a very exact way, in the act of copulation. Histological sections of the grafts show the ovary to have remained apparently functional, while the testis has undergone marked changes leading to destruction of spermatocytes and spermatozoa.—Author's Abst.

(GONADS) On the physiological properties of the gonads as controllers of somatic and psychical characteristics. II. Growth of gonadectomized male and female rats. Moore (C. R.), J. Exp. Zool. (Phila.), 1919, **28**, 409-469.

Gonads were removed from eighteen male and twenty-two female albino rats, at ages from twenty-three to thirty days. The weights of the animals were recorded for a period of 180 days, and from these records the author compiles a growth curve which shows the average weight of castrated males to be greater than that of spayed females. He concludes that there is a potential weight difference between the sexes independent of the secretion of the gonads. This fact must be borne in mind when conclusions are to be drawn regarding the effect on the growth curve of the transplantation of gonads from one sex to the other.—M. M. H.

(GONADS) Relation of the sex glands to metabolism. Murlin (J. R.) and Bailey (H.), Tr. Am. Gynec. Soc. (Phila.), 1917, **42**, 247-56.

Published elsewhere. Abst. Endocrin. **1**, 473.

(GONADS HYPOPHYSIS) The effects of inanition in the young upon the ultimate size of the body and of the various organs in the albino rat. Jackson (C. M.) and Stewart (C. A.), Anat. Rec. (Phila.), 1919, **16**, 153.

Thirty-eight litters were used; 113 rats survived, 35 male and 35 female test rats, 27 male and 16 female controls. Groups were underfed from birth to three, six, and ten weeks of age,

and from three weeks to twenty weeks or to nearly one year. Thereupon the test rats were fully refed. They grew variably, but remained permanently stunted, failing to reach the adult size of the controls. Stewart ('16) found perfect recovery after underfeeding from three to ten weeks of age. The ultimate effect, therefore, varies according to the age of the animal and the extent of the underfeeding period. This is in agreement with the results of Aron and Brüning, but disagrees with Osborne and Mendel. Forty-five of the rats (28 test and 17 controls) were autopsied. Of the individual organs, the brain, spinal cord, hypophysis, and lungs average slightly subnormal; the ovaries distinctly so. The heart and alimentary tract are slightly, and the testes and epididymides definitely above normal weight. While some abnormalities thus appear, they are usually slight, and in general the organs and parts are nearly normally proportioned in the permanently stunted rats. Thus early starvation apparently retards the later growth process of the body as a whole.—Author's Abst.

(GONADS) Un caso de distophia genito-glandular. Murillo Campos. Archivos de Biologia de San Paulo (Brazil), 1918, **3**, 324.

A case of a boy of 18 years with all the characteristics of a eunuch is described. He was beardless, had testes of almond size, and penis 6.8 cms. in length. The Wassermann reactive was negative. He had juvenile mentality.—G. P. G.

(HORMONES, AUTONOMIC N. S.) Neurocirculatory asthenia (soldier's heart). Carroll (J. H.), Am. J. M. Sc. (Phila.), 1918, **158**, 35-46.

From an analysis of the literature and a study of his own cases the author concludes: 1. That some types of hyperthyroidism are analogous to the entity neurocirculatory asthenia and their pathogenesis is probably identical, the phenomena being attributable to a hyperexcitability of the opposing sets of fibers of the autonomic nervous system. 2. That in both conditions the syndrome develops in individuals in whom there is a hyperirritability of one or other sets of fibers in the autonomic system. Hence, constitutional predisposition due to inherited sympathetic or vagotonic instability is a factor in the causation on a sound basis. 3. That nervous and emotional strain is the immediate cause, precipitating the syndrome in susceptible individuals. 4. That in the cause of susceptibility (acquired instability of the autonomic nervous system) infection plays a predominant role and the susceptibility in such cases may be accepted as indicating a chronicity of the infec-

tion with constant or frequent outpourings into the blood of the infective agent. 5. That there is a certain rationale for believing that this instability in the autonomic nervous system lies in the element of anaphylaxis in disease in the predilection of anaphylatoxin for the parasympathetic system. 6. That there is some evidence that deficiencies of calcium in the diet may have played a part in the causation of some of the phenomena and that the higher plane of inorganic metabolism in the organism may have shared with adrenin increase the responsibility in causation of the thyroid hyperplasia and hyperthyroidism among the soldiers.—R. G. H.

(HORMONES) Climacteric hypertension: a study of high blood pressure during and following the menopause. Hopkins (A. H.), Am. J. Med. Sci. (Phila.), 1919, **157**, 826-36.

A type of high blood pressure is described which develops in women at the time of the menopause, and possibly as a result of it. There is no evident arteriosclerosis, at least for several years after its onset, no renal involvement and often no symptoms of any sort for a decade or longer. Little has been written on this condition. Hopkins' paper is based on a study of 51 cases. The blood pressure in many instances was very high, reaching 230-310 systolic and 130-150 diastolic. Among the chief symptoms the gastric neurosis group are prominent, with fermentation and constipation. Nervousness and pains in the limbs are common. Headache and evidence of cardiac embarrassment are next most frequent headache in some degree being present in nearly all cases. Five of the cases are described in some detail and in contrast, two cases of renal sclerotic hypertension in men of corresponding age. The high blood pressure resulting ultimately produces a degree of vascular fibrosis. The author suggests as a probable explanation of the climacteric hypertension that the ovarian influence having diminished an endocrine imbalance ensues allowing the adrenals, hypophysis and thyroid to overfunction. It is concluded that routine blood pressure studies in all women at the period of the menopause would be of great diagnostic and therapeutic benefit for the patient's future.—R. G. H.

(HORMONES) Os hormonios e o sistema vegetativo. Gallotti (O.) Archivos Brasileiros de Med. (Rio de Janeiro), 1919, **9**, 3.

From a review of the literature it is concluded that the endocrine and the vegetative nervous systems mutually influence each other.—G. P. G.

(HYPOPHYSIS) A case of hypopituitarism. McIver (J.), J. Nerv. & Ment. Dis. (N. Y.), 1917, **45**, 443.

A clinical description of a case of hypopituitarism presenting increased sugar tolerance, polyuria, and a deep sella turcica.—F. S. H.

(HYPOPHYSIS) Acromegaly illustrating the chief features of the disease. Futcher (T. B.), Med. Clin. N. Am. (Phila.), 1917, **1**, 131-143.

A report of a case of acromegaly in a woman 67 years of age. The report gives the history and physical examination of the case, illustrating the chief features of the disease, with the possible association of a myxoedematous factor. There is also a classification of the endocrine glands from an embryologic standpoint and a discussion of the "accelerator" and "inhibitory" action of the hormones of these glands. The anatomy and histology of both lobes and pars intermedia of the pituitary gland is given, and also the functions of the two lobes. In addition, the pathology found in the pituitary in acromegaly is described. The commonest finding is hyperplasia. Adenoma, fibroma, sarcoma, and cysts are also found. The latter, Futcher thinks, result from degenerative changes in pre-existing tumors. He gives a classification of dyspituitarism and concludes the article with the treatment of acromegaly. In the last discussion he thinks that organotherapy should be followed out after hypophysectomy, since life is not compatible with complete removal of the gland. Its administration combats the somnolence and tendency to adiposity which develops owing to the increased carbohydrate tolerance. In cases where hypopituitarism dominates the picture, posterior lobe preparations should be given. Oral administration does not yield results at times and in these cases recourse may be had to hypodermic administrations of the extract.—M. M. P.

(HYPOPHYSIS) A discussion of the lipoids concerned in growth with clinical observations on the action of tethelin. Barney (E. L.), J. Lab. & Clin. Med. (St. Louis), 1917-1918, **3**, 480-486.

Following a suggestion received by the work of Robertson on the effect of tethelin in the healing of wounds in mice, B. studied its effect in the treatment in several types of indolent ulcers, all of which, with one exception, had failed to respond to the usual medication. No luetic ulcers were included in the study. The tethelin was applied either in solution on gauze or dusted as a powder on the ulcer. The results were

favorable and tethelin, a lipoid extracted from the anterior lobe of the pituitary body, is considered efficacious in the treatment of chronic ulcers.—F. S. H.

(HYPOPHYSIS) Distrofia adiposogenital. Schweizer (E.) Prensa Med. Argent. (Bs. Aires), 1917-18, **4,** 366.

Published elsewhere. Abst. Endocrin., 1918, **2,** 506.

(HYPOPHYSIS) Dwarf growth with atrophy of the anterior lobe of the hypophysis. (Zwergwuchs bei atrophie des hypophysis-vorderlappens.) Simmonds (H.), Deutsche med. Wchnschr. (Berlin), 1919, **45,** 486.

A man of 21 years, 110 cm. in height, died of purulent meningitis. His intelligence had been normal. The internal genitals were very small, the testicles being the size of a pea and the prostate the size of that of an infant. A small thymus, minute adrenals and thyroid were found. The pituitary was small, an anterior lobe was not to be found by gross examination, but upon histological examination some cells probably of the anterior lobe occurring in the first days of life may produce dwarfism.—J. K.

(HYPOPHYSIS) Emploi de l'extract d'hypophyse en obstétrique. Schwaab (M.) Presse Méd. (Paris), 1919, **27,** 299-300.

A general discussion of the use of pituitary extract in obstetrics. The author's experience has led him to the conclusion that it has an important place. With proper attention to limitations of dosage it should be used whenever either primary or secondary uterine inertia develops and when at the same time acceleration of labor is desirable in the interests of either mother or fetus. When inertia coincides with premature rupture of the membranes pituitary extract should be given immediately, especially in multiparas. Its use in postpartum urine retention is also commended. The uselessness of the drug for the induction of labor or for producing abortion is emphasized. The contra-indications for its use are given as: Cardiopathies, hypertension, arteriosclerosis and pronounced albuminuria.—R. G. H.

(HYPOPHYSIS) Experimental Studies on Growth. IX. The influence of tethelin upon the early growth of the white mouse. Robertson (T. B.), and Delprat (M.), J. Biol. Chem. (Balt.), 1917, **31,** 567-574.

The effect on growth of white mice of feeding the lipoid,

tethelin extracted from the anterior lobe of the pituitary, during the early growth periods was studied. When the substance was fed to the mothers the suckling mice showed no deviations from the normal growth rate up to the period of weaning. After that time a noticeable acceleration in growth is observed which persists until the culmination of the second and the initiation of the third growth cycle, after which a decisive retardation sets in.—F. S. H.

(HYPOPHYSIS) Extract of pituitary gland in labor. Jamieson (J. P. S.), N. Zealand M. J. (Wellington), 1915-16, **14,** 233-35.

The three outstanding benefits of pituitrin are that labor is shortened, the use of forceps obviated, and hemorrhage diminished. It is also of value in preventing tympanites and retention of urine. As to the disadvantages, Jamieson states that in proper cases, there are none. Cases, however, should be chosen with great care. Patients with flabby, dilated hearts are bad subjects, as are also eclampties. His own rule is never to inject it until the os is fully dilated, or it is felt to be readily dilatable.—E. N.

(HYPOPHYSIS) Hypophyseal dystrophy in hydrocephalus. Strauch (A.), J. Am. M. Assn. (Chgo.), 1919, **72,** 1731-34.

The case is described of a nine-year-old girl who, coincident with hydrocephalus, developed various signs of hypophyseal disorders. With rapid growth appeared mental deterioration and an asthenia which compelled the child to stay in bed or in a chair. Polydipsia and polyuria were marked. A considerable degree of obesity developed, the fat being distributed especially in the regions of the pelvic and pectoral girdles. The mons veneris and labia majora were prominent and beginning pubic hirsutes was apparent. The skin was smooth and delicate and without perspiration. Blood pressure was 95/65 and pulse, 100-110. Glucose by mouth in 100, 150 and 210 gm. doses caused no glycosuria. Roentgenograms showed enlarged, shallow sella turcica and reduced clinoid processes. A gain in weight of three pounds in two weeks was noted. The patient died of broncho-pneumonia. At postmortem there were found in the hypophysis subcapsular hemorrhages, excessive hyperemia and vascularization of the anterior lobe, hyaline or colloidal thrombosis and excessive amounts of colloid in the acini.—R. G. H.

(HYPOPHYSIS) Hypophyseal therapy in Basedow's disease. (Zur hypophysären Therapie des Morbus Basedowi). Hof-

stätter (R.), Ztschr. f. Geburtsh. u. Gynäk. (Stuttgart), 1918. **80,** 493.

The author from investigations on a series of fifteen typical cases of Basedow's disease, the clinical pictures of which are given, found that marked improvement resulted from the use of repeated injections of 1 cc. posterior lobe extract followed for a time by the oral administration of desiccated pituitary substance. From this he concludes that the anatomical changes in the thyroid after hypophyseal therapy speak for an influence of the thyroid in the sense of an inhibition of secretion with respect to the pituitary. Contraindications are pregnancy and arteriosclerosis.—F. S. H.

(HYPOPHYSIS) On the effects of ablation of the epithelial hypophysis on the other endocrine glands. Smith (P. E.) Proc. Soc. Exp. Biol. & Med. (N. Y.), 1919, **16,** 81-82.

When the epithelial hypophysis is ablated in early embryonic stages in the frog, the resulting larvae suffer in a characteristic way from defects in their pigment system. An equally definite set of alterations is produced in the other glands of internal secretion. Both Allen and the writer have reported the underdevelopment of the thyroid gland to which may in turn be attributed the failure of metamorphosis in these larvae. The posterior lobe of the hypophysis in these larvae is always present, though greatly underdeveloped—ample proof apparently of the need of coassociation with the epithelial portion of the gland. Most emphatic is the effect produced on the adrenal, whose cortical or interrenal substance is greatly decreased. This discovery was greatly faciliated by the employment of those methods which fix and stain the lipoids of the cortical tissue. These changes in the adrenal tissue do not occur in thyroideetomized larvae and are consequently not to be referred to the thyroid reduction which is coincident with them.—Quoted.

(HYPOPHYSIS) Pituitary headaches and their cure. Pardee (I. H.), Arch. Int. Med. (Chgo.), 1919, **23,** 174-184.

Pardee reviews the conditions usually accompanied with headache, after which he takes up a special set of symptoms which he calls pituitary headache, due to enlargement of the pituitary gland. This may be physiological, occurring during the menses and pregnancy or may be compensatory, due to decreased function of other endocrine glands. Various degenerations and true tumor formation are also mentioned. The symptoms are deep-seated frontal headache, localized behind the

eyes between the temples, characterized by its duration and persistency. These patients apparently have marked craving for sugars, which ultimately aggravate the symptoms. In many cases there is abnormality of the sella turcica. This form of headache, if not due to neoplastic growths, is amenable to treatment. Pardee recommends one grain of the whole gland pituitary substance three times daily.—B. T. S.

(HYPOPHYSIS) Pathogenesis and etiology of acromegaly (Sulla patogenesi ed etiologia dell' acromegalia). Massalongo (R.) and Pizza (C.) Policlin. (Rome), 1916, **23**, 42-84. Abst. Lancet (Lond.), 1916, **1**, 926.

Massalongo and Piazza publish a case which lends support to the view that acromegaly, which has its origin in hyperfunction of the pituitary gland, is often complicated by contemporary or successive phenomena dependent on functional or organic change in the other glands of internal secretion. Facts noted in the case made it impossible to exclude the presence of symptoms dependent on simultaneous changes in other endocrinous glands, especially in the thyroid and gonads. Changes in these glands do not signify their participation in the pathological processes of acromegaly, but that the endocrinic system constitutes an organo-functional whole whose constituent elements are physiologically in such intimate connection that one of them cannot undergo any changes without a reaction taking place in the others.—M. M. P.

(HYPOPHYSIS) Presentation of pathological specimen of a large tumor of the pituitary gland. Lynch (R. C.) Ann. Otol., Rhinol. & Laryngol. (St. Louis), 1917, **26**, 1127; Tr. Am. Laryngol. Assn. (N. Y.), 1917, **35**, 139-43.

See Endocrin., 1918, **2**, 502.

(HYPOPHYSIS) Relaciones entre la hipofisis y la colesterina. Goñalons (G. P.) Primer Congreso Nacional de Medicina. (Bs. Aires), 1916, **4**, 51.

Investigation of the cholesterin content of the hypophysis led to the following conclusions: The hypophysis has a considerable cholesterin content which presumably is secreted into the blood. The hypercholesterinemia of pregnancy is due not only to corpus luteum and adrenal hyperplasia as Chauffard, Grigaut and Laroche believed, but also to hypophyseal hyperplasia. The hypophysis cholesterin content was diminished in generalized sarcomatosis (two cases). The posterior lobe of a

young bull was found to contain more cholesterin than the anterior lobe. The content is higher in dogs than other animals. It is higher in men than in women. There was found hypercholesterinemia in acromegalics and in dogs after hypophysis extirpation.—Author's abstract.

(HYPOPHYSIS) Report of several cases of hypophyseal disease. Blum (H. N.), New Orleans M. and S. J., 1917, **70,** 583.

A brief clinical report of four cases showing disturbances of vision associated with deformations of the sella turcica.
—F. S. H.

(HYPOPHYSIS) Sindroma hipofisiario de origen infundibular (Pituitary Syndrome). Olaechea (M. G.), Anales de la Facultad de Med. de Lima, 1918, **2,** 103.

The syndrome described is characterized by disordered heart beat (tachycardia, extra systoles), narcolepsy, polyuria and polydipsia. It is similar to a syndrome produced experimentally in dogs by Camus and Roussy. The case described is similar to one reported by Claude and Lhermitte in 1917. The syndrome was due to a tumor in the third ventricle. Olaechea's case was that of a woman of 35. The first abnormalities noted were impaired vision, reduced sensibility in the right side of the face, mucosa of the cheek and teeth and hyperesthesia of the right side of the tongue and palate. There were deafness and exaggerated tendon reflexes on that side. Bilateral choked disk and right deviation of the head and body were noted. In ten months the blindness became total. Constipation was marked. Toward the last intense headaches and tachycardia (140 beats per minute) occurred when the patient attempted to sit up. Compression of the infundibulum was regarded as the cause of the pituitary symptoms. Death was by syncope. No autopsy was performed.—G. P. G.

(HYPOPHYSIS) Some problems in obstetrics; caesarean section, high forceps, pituitary extract. Bandler (S. W.), Am. J. Surg. (N. Y.), 1916, **30,** 121-27.

Pituitrin is said to be valuable in stimulating bladder contractions and intestinal peristalsis. Bandler, however, says that for the former condition there is little need for pituitrin on account of the ease and safety of cathetrization, if urotropin is used systematically. He lauds the use of pituitrin in post-operative tympanites. It is valuable also in post-operative cases as a stimulant, being in this respect in a class with

strychnin, caffein, digitalis and camphor. Bandler has used pituitrin in a number of cases of Caesarean section, giving it in small doses several times a day for several days after operation. As soon as the abdominal incision is made, an injection of pituitrin is given, causing strong contraction of the uterus immediately after extraction of the infant. It also stimulates the secretion of the breast. In the third stage of labor Bandler always gives ergotol, no matter how much pituitrin the patient may have had. In his experience, pituitrin has no marked action in procuring emptying of the uterus in abortion, although he uses it in practically every case. Hypodermic use of the extract he considers an excellent ambulatory treatment for menorrhagia or metrorrhagia in young girls in whom examination or local treatment is out of the question. An injection is given every day for weeks and months. Bandler states that only occasionally are patients annoyed by weakness, pallor, trembling of the extremities, etc. To patients who are sensitive to the drug, he gives the whole gland in capsules for long periods of time. During parturition the three factors to be borne in mind in the use of pituitrin are proper doses, proper intervals and proper indications. He gives one-third ampoule every half hour, from three to five minims being given for the first dose to judge its effect. It is used when conditions are normal, and when all that is needed is sufficient uterine force.

—E. N.

(HYPOPHYSIS) The control of the symptoms of diabetes insipidus by subcutaneous injections of extracts of the hypophysis cerebri (pars posterior and pars intermedia). Barker (L. F.) and Mosenthal (H. O.), Tr. Assn. Am. Physicians (Phila.), 1917, **32**, 233-49.

A careful study of a patient of 44 who suffered from marked polydipsia and polyuria (8000 c.c. daily). In addition to diabetes insipidus there was evidence of "dyshypophysism," hyperthyroidism, myoma uteri, oral sepsis, arteriosclerosis and arteriolar nephropathy. The urine was very dilute (1001-1004 sp.g.) Injections of adrenin and of "tethelin" were without effect, as were also pituitary tablets by mouth, even in large doses. Pituitary extract (posterior lobe and pars intermedia), however, resulted in normal thirst and urine output. Two injections of 1 c.c. each were required daily. A single large dose (4 c.c.) was little more efficacious than 1 c.c. and doses smaller than 1 c.c. were inadequate. The efficiency of the pituitrin was not appreciably diminished during the two months included in the history. A good bibliography is appended.—R. G. H.

(HYPOPHYSIS) The pigment changes in frog larvae deprived of the epithelial hypophysis. Smith (P. E.), Proc. Soc. Exp. Biol. & Med. (N. Y.), 1919, **16**, 74-78.

Tadpoles from which the hypophysis is removed have a characteristic silvery color. This has been ascribed to a contracted condition of the melanophore pigment cells. Smith maintains that the major role is played by expansion of another type of cells, the xantholeucophores. The article is chiefly of technical interest.—R. G. H.

HYPOPHYSIS, The relation of the—to certain clinical manifestations and the therapeutic application of its extracts. Miller (J. L.), Am. J. Med. Sc. (Phila.), 1916, **152**, 549-60.

The anterior lobe of the hypophysis is essential to life, its complete removal resulting in death and its partial removal in developmental disturbances, resembling closely Fröhlich's syndrome as observed in man. But it is only extracts of the posterior lobe that have proved therapeutically active. Strictly speaking, the active substance is present in the pars intermedia. When given intravenously or intramuscularly it affects the cardio-vascular system, kidney, uterus, urinary bladder, intestine, and the secretion of the mammary glands. In the group of clinical manifestations which may be associated with disturbance in the hypophysis and the therapeutic application of its extracts, the author considers acromegaly, dystrophia adiposo-genitalis, or Fröhlich's syndrome, possibly adiposis dolorosa or Dercum's disease, diabetes insipidus and glycosuria. These various conditions are fully discussed, especially from the viewpoint of etiology and the application of hypophyseal therapy. The author speaks also of the galactogogue action of the posterior lobe and of the more important effects on uterine musculature and intestinal peristalsis. These results are obtained with extracts of the posterior lobe. They must be given subcutaneously or intravenously to obtain results. By mouth they are inactive, like adrenalin. The paper, while not presenting anything especially new, is a well prepared resumé of our present knowledge of this subject.—E. N.

(HYPOPHYSIS) Treatment of nasal and bronchial asthma by local applications of pituitary extract. (Traitment de l'asthme nasal et bronchique par les applications locales d'extrait d'hypophyse.) Bourgeois (H.), Prog. Méd. (Paris) 1917, **32**, 37-38.

Nasal asthma is markedly relieved with no untoward effects by the insertion of a cotton pledget soaked with a solu-

tion of equal parts of hypophysin and 10% novocain into the nares. In bronchial asthma the combination of hypophysin and adrenalin gives good results, but not as striking. The latter combination is given hypodermically.—F. S. H.

(HYPOPHYSIS) Un caso distrofia adiposogenital. Schweizer. Semana Med. (Bs. Aires), 1917. **24,** 54; Prensa Med. (Bs. Aires), 1917, **4,** 366.

See Endocrin., **2,** 506.

(HYPOPHYSIS) Upon the experimental exchange of skin transplants between normal and albinous larvae. Smith (E. P.) Proc. Soc. Exp. Biol. & Med. (N. Y.), 1919, **16,** 80-81.

Hypophysis-free tadpoles present a silvery appearance due largely to the expanded condition of the xantholeucophores. It is possible by working rapidly to graft skin from these albinous to normal larvae. Within 15 minutes the light skin of the graft begins to assume the darker color of the host, and within four hours the change is complete. This is interpreted as indicating that the preceding expansion of the leucophores was due to some hormone.—R. G. H.

(HYPOPHYSIS THYROID) Hypophyseal treatment of Graves' disease (Hypophysäre Therapie des Morbus Basedowi). Hofstätter (R.), Ztschr. f. Geburtsh. (Stuttgart), 1918, **80,** 493.

In 15 cases of Graves' disease in which ovarian function was disturbed (amenorrhea and dysmenorrhea following ovarian extirpation) hypophysin was given. Although favorable results in such cases have been reported by others, Hofstätter saw no effects on the chief symptoms except that some improvement occurred in cases having marked "sympathicotonia." Hypophysin has an influence on blood pressure and on the nervous system; it inhibits the function of the thyroid but stimulates the ovaries and the adrenals. This possibly explains the effects in "sympathicotonia." Hypophysin is contra-indicated in pregnancy, arteriosclerosis and Bright's disease.

—J. K.

(HYPOPHYSIS) Variaciones dela sangre en los animales privados de hipofisis (Blood changes in animals after experimental hypophyse extirpation). Goñalons (G. P.) Primer Congreso Nacional de Medicina, 1916, **4,** 52.

The investigation was carried out on the animals operated

upon by Prof. Houssay. The blood for study was taken from puppies and adult dogs, operated and control. It was found that in animals deprived of the hypophysis the blood acquired all the characteristics of that of a young animal. The number of red corpuscles and percentage of hemoglobin were diminished, but the polyneutrophile and eosinophile cells were increased by 10 per cent.—Author's Abstract.

(INFANTILISM) Chronic nephritis with infantilism. Hill (L. W.), Am. J. Dis. Child. (Chgo.), 1919, **17**, 274.

In a review of nephritis in children, Hill states that there have been twenty to thirty cases of chronic nephritis with infantilism reported in the literature. This condition may be likened to chronic interstitial nephritis in the adult. It develops insidiously and is of unknown etiology. It sometimes occurs in several members of the same family. One interesting point in the symptomatology is that these children usually show infantilism, a child of 10 or 12 years being developed mentally and physically only as much as a normal child of 5 or 6. The patient is subject to headache, the vision is poor and there is often a marked albuminuric retinitis. The blood pressure is very high, often over 200, and the heart may show considerable hypertrophy. The urine is large in amount and of low specific gravity, containing usually a very small amount of albumin and an occasional cast. The functional tests are low and the kidneys at necropsy are of the usual contracted type seen in the corresponding condition in adults. The prognosis is bad.—M. B. G.

(INTERNAL SECRETIONS) Circumscribed edema. Christofferson (N. R.) Ugeskrift for Laeger (Copenhagen), 1919, **81**, 381-407.

Christofferson discusses the pathogenesis of Quincke's circumscribed edema, and describes various experiences which, in connection with the "war edema," seem to indicate that the internal secretions have more to do with it than has been suspected hitherto. In a case described in detail the little girl had been having hemorrhagic purpura, and the blood pressure was abnormally high. Transient edema developed in different regions in turn, and a marked tendency to retention of water and salt was evident although there was nothing in heart or kidneys to explain this tendency to edema. In this and other cases in his experience, he never found anything to suggest a peculiarly unstable nervous system.—J. Am. M. Assn., **72**, 1504.

(INTERNAL SECRETIONS) Defective development of the blood. Pittaluga (G.) Arch. españoles de ped. (Madrid), 1918, **2,** 513.

The author classifies a group of blood cases as hemodystrophies. This represents groups in which the biochemical abnormalities predominate over the histopathologic, and a neuropathic factor is manifest, either directly or through the mediation of the endocrine glands. A hereditary influence is apparent. The group contains the so-called hemorrhagic diatheses, purpuras, scurvy, hemophilia, paroxysmal hemoglobinuria and hemolytic jaundice.—Physiol. Abst., **4,** 43.

INTERNAL SECRETIONS, Glands of—. Crispin (A. M.) Siglo Med. (Madrid), 1918, **64,** 908; Rev. Assoc. Med. Argent., 1918, **27,** 845.

See Endocrin., **2,** 165.

INTERNAL SECRETIONS in obstetrics and gynecology. Bandler (S. W.), Am. J. Surg. (N. Y.), 1917, **31,** 156-162.

General discussion of the functions of the ovary, thyroid, hypophysis, etc., as glands of internal secretion and the part they play in medical practice.—F. S. H.

INTERNAL SECRETIONS, Relation of—and faulty metabolism. Keister (B. C.) Virginia M. Month. (Richmond) 1918, **45,** 38-43.

Published elsewhere. Abst. Endocrin., 1919, **3,** 80.

(INTERNAL SECRETIONS) Sexual precocity in the male. Strauch (A.), Am. J. Urol. (N. Y.), 1918, **14,** 116-20.

Published elsewhere. Abst., Endocrin., 1918, **2,** 176.

(INTERNAL SECRETIONS) Sugar tolerance in cancer. Rohdenburg (G. L.), Bernhard (A.) and Krehbiel (O.) J. Am. M. Assn. (Chgo.), 1919, **72,** 1524.

The authors incidentally remark that not a few investigators have attributed cancer to faulty endocrine functioning, different glands being held responsible. So far positive proof is lacking. There are no specific lesions demonstrable in the endocrine glands of mice with spontaneous tumor nor does extirpation or the feeding of one or more of these glands have any apparent influence on the rate of growth, infectivity, or immunity against animal tumors.—R. G. H.

(INTERNAL SECRETIONS) Remarks upon the vegetative nervous system and the internal secretions. Farnell (F. J.), J. Ment. Sci. (Lond.), 1917, **63**, 225-237.

A general discussion of the interrelations between the vegetative nervous system, the glands of internal secretion and mental disturbances.—F. S. H.

INTERNAL SECRETIONS, Some clinical aspects of—. Illustrated. Bainbridge (W. S.), Hosp. Bull. Dept. Pub. Char. (N. Y.), 1917, **1**, 12-58.

An extensive and comprehensive clinical presentation with many illuminating illustrations of the more striking appearances occurring in disorders of the glands of internal secretion. Among the types pictured in the sixty-two illustrations are: dystrophia-adiposa-genitalis, adiposa dolorosa, progressive muscular dystrophy, osteomalacia, hirsuitism, microsomia, acromegaly, gynecomastia, Addison's disease, hydrocephalus, microcephalus, hyperthyroidism, and hypothyroidism.—F. S. H.

INTERNAL SECRETIONS, The relationship of the—to gastrointestinal diseases. Editorial, N. Y. Med. J., 1919, **109**, 774.

While enough is not absolutely known with regard to the internal secretions to warrant any dogmatic statement as to the exact part they play in the working of the human mechanism, it may be said that they wield a remarkable influence on physical and mental health. It may then be justly inferred that the diseases and disorders of the gastrointestinal tract are owing, at least to some extent, to the impaired or imperfect action of not only the thyroid gland, but of those internal secreions which are connected with the alimentary tract. The internal secretions should always be considered in the prevention and treatment of gastrointestinal diseases and disorders.
—H. W.

(MONGOLISM) Mongolismo. Meirelles (E.) Archivos Brasileiros de Medicina de Rio de Janeiro (Brazil), 1918, **8**, 738.

Three cases of mongolism without autopsy. Meirelles states that it is not easy to determine whether this condition is due to endocrine dysfunction or to cerebral injuries.
—G. P. G.

MAMMARY GLAND, Studies on the—. Myers (J. A.) Am. J. Dis. Child. (Chgo.), 1919, **17**, 311.

The experimental animals in this series were rats of both

sexes ranging in age from birth to ten weeks. The author arrived at the following conclusions: Severe inanition retards the growth of the milk ducts of the female rat during the first week, but apparently does not completely stop their growth. The nipple grows very little during inanition. The subcutaneous fat that appears very early in the neighborhood of the milk ducts becomes greatly decreased after the amount of food is reduced to a minimum. In all, the retardation in the development of the mammary gland is roughly proportional to the retardation in body weight (at least within limits of normal variability). When the animal is refed, the glands respond slowly. When the body weight during refeeding reaches that of a normal rat at the age of puberty, the milk ducts are far behind those of the normal rat at corresponding body weight. That this stunting is not permanent is shown by the fact that the ducts ultimately attain the same stage of development as those of a normal animal, but at a much later date.—M. B. G.

MUSCULAR DYSTROPHY, A case of—. Anon. Guy's Hosp. Gaz. (Lond.), 1917, **31,** 250.

An illustrated clinical description without explanation of etiology, of a case of muscular dystrophy.—F. S. H.

NEURASTHENIA, A form of—, due to hypoadrenia. Williams (T. A.) Am. Med. (Burlington, Vt.), 1917, **12,** 582-86.

Williams believes that neurasthenia is hypoadrenia, basing this conclusion on the apparent identity of the symptoms in the two conditions. Several cases are reported as illustrative of the results of adrenal therapy in neurasthenia. The author concedes that not all cases do well with this form of treatment. —E. N.

(OVARIES) Experimentelle Kastration durch Cholin. Wintz (H.), Arch. f. Gynäk. (Berl.), 1919, **110,** 397.

The influence of X-rays on the body cells has been much discussed. Schwartz has emphasized the statement that in tissues exposed to these rays an increased amount of cholin is found. He thinks this is due to decomposition of lecithin, Werner has reported that rabbits can in effect be castrated by the administration of cholin. The experiments were extended to the human species—especially in myoma of the uterus and in severe hemorrhages preceding the menopause. Wintz has repeated such experiments in hares and in women. In hares one ovary was removed as a control and then different quantities of cholin (in combination with boric acid) were injected.

Some of the animals became sterile, but one gave birth to young several months later. In women injections of borocholin caused atrophy of the ovaries, the degree depending upon the quantity administered. Cholin, it is concluded, has the same action as X-rays, but results are obtainable much less rapidly.

—J. K.

OVARIES, Histological examination of the—in mental disease. Forster (Laura), Dementia Precox Stud. (Chgo.), 1918, **1**, 79-91.

See Endocrin., 1918, **2**, 512.

OVARIES, Influence of the—upon the production of artificial deciduomata; confirmatory studies. Corner (G. W.) and Warren (S. L.), Anat. Rec. (Phila.), 1919, **16**, 168.

Leo Loeb reported in 1907 and 1908 that at certain stages of the reproductive cycle of the female guinea-pig, injury to the uterine mucosa leads to the formation of a tumor at the site of trauma which closely resembles in cellular structure the maternal portion of the placenta. This reaction can be elicited only during a period of two to nine days after ovulation; it does not occur in the absence of the ovaries, even if these be left in place until after ovulation has occurred. From these facts Loeb believes that the young corpus luteum formed at the time of ovulation develops a hormone which in some way sensitizes the uterine mucosa in time to receive the ovum and to participate in placenta formation. The artificial stimulus of his experiment merely imitates the trophic action of the early embryonic ectoblast. Confirming evidence was reported by Robert Frank ('11), using rats.

Pregnant animals were allowed to give birth, in order to fix the date of ovulation, which invariably occurs in rats within twenty-four hours after parturition. Six to seven days after ovulation the abdomen was opened under ether anesthesia and the uterus traumatized by the insertion of a small foreign body, such as a fine short piece of glass, into the lumen; by the passage of a silk suture through the uterine wall, or merely by scratching the mucosa with a needle inserted through the wall. In seven animals killed four or five days after operation, the traumatized areas presented large, soft, solid enlargements of dark congested appearance, more than twice as thick as the intervening parts of the uterus. In color and texture the tumors greatly resembled the enlargements of early pregnancy in the rat. Microscopic sections showed the uterine mucosa to have been replaced by a solid mass of cells varying from spindle-shaped to large oval outline. Many nuclei were

in mitosis; an occasional cell was polynuclear. In some specimens small local areas of degeneration were seen. Even when the traumatizing object had been left in place, the microscope showed not the familiar foreign-body reaction of tissues in general, but true decidual cells.

Seven other rats were treated in exactly the same way, except that shortly after ovulation the ovaries were removed. On the seventh or eighth day the uteri were traumatized, and four or five days after the second operation the rats were killed. In none did any enlargement at the site of trauma take place. In two animals the ovaries were merely separated from the uterus by cutting between ligatures near the tubal extremities of the uterine horns. In these the placenta-like tumors developed, showing that the influence of the ovaries is exerted through the bloodstream or possibly the nervous system. It is hoped that it might be possible to elicit deciduomata in rats deprived of their ovaries immediately after ovulation if early corpus luteum tissue from another species were provided. The administration of corpus luteum of the sow to a small series of rats, by mouth in the fresh state, by abdominal injection after desiccation, or in alcoholic extract, has so far given negative results.—Author's Abst., abbreviated.

OVARIES, The function of the—after X-ray treatment. (Beitrag zur Kenntnis des Verhaltens der Eierstockfunktion nach der Röntgentiefentherapie.) Werner, Arch. f. Gynäk. (Berlin), 1919, **110**, 434.

Though in young individuals sterility occurs after exposure to X-rays, there is no reason not to treat them with X-rays when necessary. Nearly always the sterility is temporary and in most cases menstruation and even pregnancy returns some months after treatment has been discontinued.

—J. K.

(OVARIES) The vertigo of the menopause. Sanes (K. I.) Am. J. Obst. (N. Y.) 1919, **79**, 7.

Vertigo is seldom the only prominent symptom of the menopause. Invariably vertigo at this time is accompanied by such disturbances as hot and cold flashes, cold perspiration, blurred vision, flickering before the eyes, headache, nausea and tinnitus. In a study of 102 cases of vertigo occurring at the menopause and not complicated by cardiovascular or renal diseases, the author found that 45 or 46 per cent had a systolic blood pressure above 150 mm. Hg. A preparation of ovarian extract was administered, each grain of which represents a grain of the fresh ovarian substance. Five-grain doses two or

three times a day were given. Larger doses were of doubtful advantage. Under this treatment 37 per cent showed marked improvement and 25 per cent were held in control. Referring to Hallion's law, the author states that "by the administration of ovarian substance, while the ovaries are still functionating somewhat, we not only supply a substitute for the internal ovarian secretions but stimulate the ovaries to an increased production of it. If this is correct the earlier in the menopause the ovarian substance is given, the better should be the results." In some cases an additional dose of thyroid seems to help in the management of the menopause. This is in accord with the idea of pluriglandular disturbance following dysovarism. The author justly laments and criticises the lack of standardization of ovarian extracts.—H. W.

(OVARY) Brain and ovarian function in mammals (Il cervello e la funzione ovarica nei mammiferi). Carlo Ceni, Arch. di fisiol. (Firenze), 1917, **16**, 1-20.

A continuation in dogs of earlier work on birds. Extensive lesions of the cerebral cortex were followed by immediate changes in the ovarian parenchyma, analogous to those already described in birds, which are attributed to "visceral shock." The more advanced Graafian follicles undergo involution. The ova atrophy showing pigmentation of the nucleus and disarrangement of the chromosomes. Physiol. Abst., **4**, 140.

OVARY, Cholesterin and—. Goñalons (G. P.) Primer Congreso Nacional de Medicina (Bs. Aires), 1916, **4**, 22.

Assays were made by Grigaut's colorimeter method with certain modifications by the author. It was found that the cholesterin content of the corpus luteum in the pregnant heifer was high (ranging up to 57 per cent); that it was higher than the ovary alone (43 per cent of fresh organ); that the blood cholesterin content diminished in castrated animals (rabbits), and that it was increased in women from whom the ovaries were removed three or four years before.—Author's abstract.

OVARY: CORPUS LUTEUM. General considerations. Osborne (O. T.), N. Y. Med. J. (N. Y.), 1918, **108**, 401.

A general paper dealing with the functions of the ovary.

(OVARY CORPUS LUTEUM) Symptoms caused by administration of ovarian and corpus luteum substance. Osborne (O. T.), N. Y. Med. J. (N. Y.), 1918, **108**, 447.

Ovarian feeding may lower a high menopause blood pres-

sure; it may awaken to energy a lackadaisical woman; it may cause menstruation in simple amenorrhea, but in this condition it is not as valuable as is corpus luteum. Toxic symptoms are rarely caused by feeding ordinary doses of ovarian extract. Corpus luteum is an active physiological and at times a toxic preparation. It may cause menstruation in amenorrhea, but it probably cannot cause abortion. It readily causes nausea, and even vomiting, when fed in too large doses or for too long a time. It lowers the blood pressure. Corpus luteum extracts may cause a little dizziness or faintness. This is especially true if they are allowed to lower blood pressure too much. The extract may cause loss of weight, but it should not be used for this object; thyroid extracts are safer and better for this purpose. There is probably no great difference between the action of corpora lutea of pregnancy and of those of nonpregnant animals. Commercial preparations of corpora lutea are of a mixed variety, and the only correct dose is that sufficient for results. If an ovarian transplant lives and functions, it should be remembered that it periodically swells, and hence, in tense, nondilatable tissue may cause severe pain.—H. W.

OVARY, Hernias of the—of the fallopian tube, and of the ovary and fallopian tube. Heineck (A. P.), Med. Times (N. Y.), 1919, **47,** 161-64.

A paper dealing with diagnosis and treatment.—H. W.

(OVARY) Melanosarkome der Ovarien. Herzog (T.) Ztschr. f. Geburtsch. (Stuttgart), 1918, **80,** 576.

Not of endocrine interest—J. K.

(OVARY) Mucous colitis (Colica Mucosa). Foges (A.) Wiener klin. Wchnsch., 1918, **31,** 1295.

The author argues for a relationship between the ovary and mucous colitis. In a single case attacks of this malady occurred always one week before the beginning of menstruation. The treatment must be the same as for dysmenorrhea. —J. K.

(OVARY) Osteomalacia. (Über Osteomalacie, eine innersekretorische Studie). Scipiades (E.), Ztschr. f. Geburtsh. (Stuttgart), 1919, **81,** 156.

It is possible by total extirpation of the thymus in puppies to get changes in the bone structure as seen in osteomalacia. By theoretical speculation the author tries to prove that the

cause of osteomalacia is in the thymus. It is an interesting article.—J. K.

(OVARY) Ovarian grafting. Bell (N. B.) Brit. M. J. (Lond.), 1918, **1**, 619.

Bell insists that the grafts must be autoplastic, small in size and from the interior follicles. The operation is not indicated in women over 42, in women sexually inactive, or in cases where conservation is at all possible. Grafts were stored in the utero-vesical pouch until the later stages of the operation, and were embedded either in the abdominal wound, drainage wound, or in the fundus of the uterus, according to the variety of case operated on. After-histories in a series of 20 cases were noted as regards (1) absence of menopausal symptoms, (2) persistence of menstruation, and (3) general health. —M. M. P.

(OVARY) Ovarian organotherapy. Graves (W. P.), Med. Clin. N. Am. (Phila.), 1918, **2**, 935.

Graves has used ovarian substance in three forms: (1) ovarian residue, a dried preparation from the ovaries of pregnant animals, with the corpus luteum excluded. (Parke, Davis & Co.) This is also put up in ampoule form for hypodermic use. (2) Extract of the whole ovary (Armour's). (3) Extract of corpus luteum (lutein tablets of Hynson & Westcott). These three preparations have been, so far as his experience goes, the most efficacious. The respective therapeutic value of the three forms has, in general, proved in the order named. "This conclusion is not without rational theoretic confirmation. There is scientific evidence to show that the chief source of the ovarian internal secretion is in the so-called interstitial cells. These cells have their origin in the connective tissue envelope of the follicles, and are developed both in the process of follicle atresia and in corpus luteum formation. Therefore preparations from the ovarian stroma alone and from the corpus luteum alone both possess therapeutic value." The use of ovarian residue of pregnant animals was the result of his personal experimentation. He found in cases in which corpus luteum was left in the ovary and those in which it has been enucleated, that the latter gave better results. The cases cited are those of hysterectomy with ablation symptoms, symptoms of menopause, and irregularities of menstruation.—M. M. P.

(OVARY) Ovarian salvation vs. ovarian destruction. Bizot (A. R.), Am. J. Surg. (N. Y.), 1919, **33,** 134-40.

From a review of recent literature Bizot concludes that in all cases of doubt one ovary of women of child-bearing age should be conserved except in the presence of undoubted malignancy. Sterilization can not be effected always by leaving an ovary on one side and a tube on the other. Neither can both tubes be removed, leaving part of an ovary, with assurance of sterility. Under no circumstances should both ovaries be removed as a matter of mere prophylaxis.—R. G. H.

(OVARY) Relation of blood lipases to cell metabolism (Die Bedeutung der Blutlipasen für die Fettstoffwechsel der Zellen). Bayer (G.) Ztschr. f. Biol. (Münch. u. Berl.), 1919, **69,** 365.

The lipolytic power of the blood serum was found to be much lower in female frogs than in males. When ovarian extract is administered the lipolytic power is diminished—J. K.

OVARY, Relation to the—to the uterus and mammary gland from the experimental aspect. Loeb (L.) Tr. Am. Gynec. Soc. (Phila.), 1917, **42,** 172-207.

Published elsewhere. Abst. Endocrin., **1,** 514.

(OVARY) Papillary cystadenoma of the ovary. Corcia (J.) N. Y. Med. J. (N. Y.), 1918, **108,** 837-38.

Case report of an unmarried woman, 32 years of age, in the peritoneal cavity of whom an operation disclosed about five gallons of fluid and an extraordinary number of cysts of different sizes. These surrounded with racemose disposition a central and large cyst containing more than a gallon of fluid. On the external and internal surfaces of these cysts were numerous papillomata which extended also into the peritoneum, intestines, bladder, and to the ovary on the other side. After tapping the central cyst the whole mass was removed. The cyst originated on the left side, but no trace of the ovary could be found. The right ovary was also removed. It also was studded with papillary growths and a few cysts. The patient made an uneventful recovery. Seven years after the operation the patient was enjoying good health.—H. W.

OVARY Sarcoma of the—in a child twenty-three months old. Hayd (H. E.) Abst. Proc. Am. Assn. Obst. and Gyn., N. Y. Med. J. (N. Y.), 1918, **108,** 968-69.

Report of a case of small round cell sarcoma of the ovary in a child 23 months old.—H. W.

(OVARY) Theory and treatment of osteomalacia (Zur Theorie und Therapie der Osteomalazie). Cramer, Deutsche med. Wchnschr. (Berlin), 1919, **45**, 475.

The fact that osteomalacia in pregnancy may be cured by castration proves that defective lime metabolism of the foetus is not the cause of this disease. Most probably the cause is an enormous increase of the internal secretion of the ovary caused by the internal secretion of the corpus luteum. Transplantation of an ovary has a much more striking effect when it is transplanted with a corpus luteum than without. A good result is seen in osteomalacia from the administration of milk of castrated goats.—J. K.

(OVARY) The corpus luteum in its relation to amenorrhea, sterility, abortion, and pseudo extra-uterine pregnancy. Oehsner (E. H.), Illinois M. J. (Chgo.), 1919, **35**, 225-26.

Observations made by veterinarians in the past few years indicate that if a false corpus luteum remains unabsorbed in either ovary of the cow, she remains sterile. This condition corresponds to amenorrhea in women. Expressing this false corpus luteum or allowing it to be absorbed, causes oestrus to reappear. Women who are sterile and have not menstruated should be examined by laparotomy for an unabsorbed corpus luteum. Veterinary surgeons have discovered that in trying to express a false corpus luteum they sometimes rupture a true corpus luteum, causing the death of the cow by hemorrhage or an abortion within twenty-four hours. This observation throws light on some obscure problems in gynecological surgery, such as the finding of blood in the peritoneal cavity, ascribed to extra-uterine pregnancy, although no placental tissue is found. Experience has led me to believe that post-operative abortions are due to trauma of the corpus luteum and not of the uterus. By being very gentle with the ovaries during operations on pregnant women I have found it possible to avoid abortion, the women going to full term.—Author's Abst. (abbreviated).

(OVARY) The formation of the corpus luteum (Untersuchungen über die Bildung des Corpus luteum und die Follikelatresse). Borell (H.) Beitr. z. pathol. Anat. (Jena), **65**, 108.

Of no endocrine interest.—J. K.

OVARY, The internal secretion of the—in osteomalacia. (Zur inneren Sekretion der Ovarian bei Osteomalakie). von Franqué. Deutsche med. Wchnschr. (Berlin), 1919, **45,** 424.

Though it is demonstrated that osteomalacia can be cured by removal of the ovaries, this does not prove that in osteomalacia there exists an abnormal function of the ovaries. It is as likely that the adrenals functionate too little. Then the ovaries produce too many antagonists. The removal of the ovaries may have the same result as an increase of the adrenal functions. The author promises to publish a long article on this question in the Centralblatt für Biologie.—J. K.

(OVARY) The menopause. An analysis of two hundred cases. Norris (C. C.), Am. J. Obst. (York, Pa.), 1919, **79,** 767-78.

Menstruation depends upon an ovarian secretion, hence the menopause is due to alterations in ovarian function. The menopause is established in women of the Eastern United States at 46 to 49 years, and not 42 to 45 as usually stated. The age at which the menopause appears varies within wide limits. Menstrual function is prolonged by child-bearing, marital relations, good nutrition and hygiene, city life and education; converse conditions tend to an earlier menopause. Climate and race probably play but a small part in the age at which the menopause appears. Hereditary influences are marked in some families. In most cases the chief feature of the menopause is not the diminution or cessation of bleeding, but the neuroses. These frequently antedate any change in the menstruation and may continue from 6 to 18 months after the final cessation of flow. The menopause should be established without the loss of blood. In about 90 per cent of absolutely healthy women the menopause occurs normally, but among average women 30 per cent present symptoms which call for a careful physical and gynecological examination.—H. W.

OVARY, Transplantation of the—in women and animals (Ovarien-transplantationen bei Menchen und Tieren. Cramer, Deutsche med. Wchnschr. (Berlin), 1919, **45,** 475.

No new data are brought forward.—J. K.

(OVARY) Types of tubo-ovarian suppuration and their treatment. Green (R. M.) Boston Med. and Surg. J., 1919, **180,** 179.

A paper of clinical interest dealing with the differentiation, classification and treatment of tubo-ovarian suppuration. —H. W.

(OVARY) Vertigo of menopause. Sanes (K. I.), Abst. Proc. Am. Assn. Obst. and Gyn., N. Y. Med. J. (N. Y.), 1918, **108,** 967-68.

Menopause vertigo is mainly of the objective type, i.e., a sense of rotation of the visible or palpable environment. Some demonstrate subjective vertigo, i. e., sensations of motion of the body itself. Vertigo is seldom the only prominent menopause symptom; it is almost always accompanied by such disturbances as hot and cold flashes, cold perspiration, palpitation, blurred vision, flickering before the eyes, headache, nausea, and tinnitus.—H. W.

(PANCREAS) Agents which accelerate glucolysis (Les agents qui activent glycolyse). Lépine (R.) Arch. Physiol. Path. Gen. (Paris), 1918, **17,** 747-71. Physiol. Abst., **3,** 378.

In the absence of bacterial infection and other sources of error, upon warming the sugar disappears from the blood of a depancreatized dog more slowly than from that of a normal animal. Stimulation of the nerves to the pancreas or ligation of its duct produces increased glucolysis in blood withdrawn thereafter; this is due to rise of pressure in the small ducts and increased absorption of the internal secretion of the pancreas. The greater portion of this internal secretion goes to the lymphatics. The utilization of sugar depends on two distinct substances which are present in all tissues: (1) an intracellular enzyme which decomposes the sugar molecule and (2) a thermostable substance, produced chiefly but not exclusively, by the pancreas, and functioning as activator of the intracellular enzyme. The blood decomposes glucose more easily than other sugars; various products, including lactic acid, are formed; production of glucuronic acid is a special, not a normal type of glucolysis. Chem. Abst., **13,** 1224.

(PANCREAS) The effect of pancreatectomy on the catalase content of the tissues. Kennedy (J.) and Burge (W. E.), Arch. Int. Med. (Chgo.), 1917, **20,** 892-895.

In dogs it was found that extirpation of the pancreas decreases the catalase content of the liver by about 75 per cent, which results in decreased output of the catalase into the blood and hence a lessened supply to the tissues. The decreased catalase content of the tissues may account for the imperfect or defective oxidation in diabetes, since the amount and intensity of oxidation is so inseparably linked with catalase.—F. S. H.

(PARATHYROIDS) Tetania enurética. Busco (J.) Prensa Med. Argent. (Bs. Aires), 1917-18, **4**, 366.

Published elsewhere. Abst. Endocrin., 1919, **3**, 87.

PARATHYROIDS, Transplantation of—in post-operative tetany (Epithelkörperchenverpflanzung bei postoperativer Tetanie). Thierry (H.), Münch. med. Wchnschr., 1919, **66**, 538.

Two cases are described in which post-operative tetany was cured by homoplastic transplantation of parathyroids into the preperitoneal fat. The author prefers in such cases to use the parathyroids of women operated upon for goitre. Surgical details are given.—J. K.

(PINEAL BODY). Further evidence in support of the glandular nature of the pineal body. Tilney (F.), J. Nerv. & Ment. Dis. (N. Y.), 1917, **46**, 442.

Comparative histology and ontology of the pineal body furnishes tenable evidence that this structure is a gland.

—F. S. H.

(PINEAL) Further experiments with pineal gland extract. Goddard (H. H.), J. Am. M. Assn. (Chgo.), 1917, **68**, 1340.

Goddard reports the further observations on one of the patients who had been in his original series of feeding experiments with this gland. This was a girl, 8 years old, with a mentality of 3 when he began the experiment. At the close of the series, she tested 4 years, which was a gain of one year mentally in four months. Because of the good results in her case, she was selected for further tests. She was observed, weighed, tested under her ordinary institutional environment and then brought to the laboratory to live. Here she was given a special diet and the observations continued. After her normal curve had been established, she was fed pineal gland for six months and then the gland was discontinued and she was observed for another period. At the time of reporting, it was 15 months since the second experiments had ceased and 20 months since the administration of the gland. There was no marked change in her growth curve during the period of administration nor was there any other effect as far as physical condition shows. There was no change in the mentality since March, 1912, when she tested 5 years. Goddard feels that the influence of the pineal gland in this case was nil. He also conducted further observations on cases of Mongolian idiocy.

Two cases of this type were selected. One was 10 years old with a mentality of 4, the second was 9 years with a mentality of 3. The first was given the gland for 6 months, while the second received it for 12. For the first month, they were both given one capsule once a day, this then being increased to twice a day. The results obtained confirmed those of the first series in demonstrating that this gland had no effect on Mongolian idiocy.—M. B. G.

(PINEAL) The morphology and evolutional significance of the pineal body. Tilney (F.), and Warren (L. F.), Am. Anat. Memoirs (Phila.), 1919, **No. 9,** 1-257.

The comparative morphology of the diencephalic roof is carefully reviewed, and the epiphysis studied in detail with special reference to its evolutional significance. The authors point out that, as a whole, the region is fundamentally glandiferous. The epiphyseal complex (pineal and para-pineal bodies) exhibits a pluripotential tendency. In lower forms the tendency towards the formation of a visual organ is shown, while in higher vertebrates the complex has glandular characters. The development towards a sensory organ is seen only in the end vesicle, while the proximal portion is always glandiferous. It is this proximal portion which shows the greater phyletic constancy, and a progressive development from the ophidians up through the mammals. Even in lower forms it is composed of cells which appear to be secretory. This glandiferous tendency is the fundamental inherent tendency of the complex, as of other parts of the diencephalic roof; while the differentiation towards a visual organ is an adaptive modification occurring in a few forms.

The gland contributes its secretion to the cerebro-spinal fluid in lower vertebrates, but in the higher forms it is endocrine. Its histology is considered in detail. In the mammals studied by the authors, the parenchyma consists of large cells with extensive cytoplasm and vesicular nuclei, arranged in acini or cords. Scattered among these are smaller cells, some of which have large, deeply staining nuclei and others pale nuclei and many cytoplasmic granules. In the early stages of differentiation the parenchmya cells have a relatively small amount of cytoplasm, giving the gland the appearance of lymphoid tissue. Later, the cytoplasm increases and the glandular nature of the cells is evident.—M. M. H.

(PITUITRIN) De l'extrait de lobe posterieur de l'hypophyse en obstetrique. Chenerson (M.) Arch. mens. d'Obstet. et de Gynec. (Paris) 1918, **7,** 22.

The use of that amount of extract representing 0.2 gm. of dried gland is advocated as the optimum dose. In simple uterine inertia and in cases of retarded labor with ruptured membranes 88 per cent of the cases responded to pituitary treatment. Favorable effects were also often obtained in the suppression of the hemorrhages of labor. The post-partum urine retention is overcome by the use of extract of the posterior lobe of the hyophysis. The author considers that the extract should not be used to initiate labor, but only for the purpose of hastening delivery.—F. S. H.

PITUITRIN, Does the administration of—to the mother produce diffuse nervous lesions in the infant? Heard (A. G.) Texas State M. J. (Fort Worth), 1916, **12**, 264-66.

Heard quotes Norris, Bandler, Mosher, Mundell and others to emphasize the danger, both to mother and child, which may arise from the obstetrical use of pituitrin. It is recognized by all authorities that birth injuries are etiological factors in the production of infantile cerebral palsies. Any factor producing increased or undue pressure on the foetal head is a strong predisposing cause of cerebral or meningeal hemorrhage. Pituitrin improperly used, either as to dosage or time, produces uterine contractions of such force that rupture or tetanus of the uterus is a not infrequent accident. Such force as this must enormously increase the pressure on the foetal head, particularly when labor is rendered so precipitate that molding cannot take place and gradual dilatation of the birth canal cannot occur. Heard reports three cases of extensive cerebral or meningeal hemorrhage of the new born, undoubtedly due to birth injury. In two of these the striking clinical feature was the occurrence of convulsive attacks. In the third, the child, then thirteen months old, was in almost constant motion, turning and twisting the head from side to side; he had no use of arms or legs, and was fed with great difficulty. He appeared to be entirely blind and the pupils were dilated and unresponsive to light. In no case was the child a first-born; in no case was there constitutional disease in either parent or child; in no case was there any question of prolonged or difficult labor; in each case a precipitate delivery was effected by the exhibition of pituitrin early in labor with the consequent induction of violent uterine contractions. Two additional cases of the same general type are reported by Bubis.

The conclusions are as follows: 1. That the improper use of pituitrin extract in labor is a cause of cerebral or meningeal hemorrhage in the new born. 2. That hemorrhages in the nervous system of infants, resulting from the use of pituitrin in

labor, are productive of diffuse nervous lesions, so extensive as to result in early death, or, if the child survives, in paralysis, epilepsy or idiocy. 3. That cases representing nervous lesions resulting from birth injuries should be carefully investigated as to the possibility of pituitrin having been effective in their causation.—E. N.

PITUITRIN in labor. Matheson (F.), N. Zealand M. J. (Wellington), 1915, **14**, 294.

The greatest objection to the use of pituitrin is the difficulty of judging what its action will be in any particular case. Once given it is beyond control. While it hastens the third stage of labor, the rapid detachment of the placenta may result in small pieces being retained. If delivery does not occur in about one hour after pituitrin has been given, there may be uterine relaxation with postpartum hemorrhage. Matheson believes that forceps delivery is preferable to the use of pituitrin. He restricts the use of the latter to multiparous women in whom the perineum has lost its rigidity, and in the third stage of labor to those cases with a tendency to hemorrhage.—E. N.

(PITUITARY) The use of pituitary extract for the induction of labor. Adair (F. L.) Interstate M. J. (St. Louis), 1916, **23**, 1111-15.

Pituitary extract is of value in bringing on labor in premature case in some instances and is worth a trial when it is not necessary to end the pregnancy rapidly. In cases of ruptured membranes it is of value in initiating uterine contractions. In placenta marginalis or lateralis, when the membranes rupture or are ruptured artificially, pituitrin is of value in starting uterine contractions and may save the necessity of intrauterine manipulations. Pituitrin should be used in cases that have gone over time before any other method of inducing labor is resorted to, except in cases where its use is contraindicated or it is necessary to terminate pregnancy rapidly.
—H. W.

(PITUITRIN) Milk production and drugs. McCanlish (A. C.) J. Dairy Sci., 1918, **1**, 475-86.

Numerous drugs were tried. Individual cows vary greatly in their responses. No drug was found to be relied upon to increase milk and butter production. Pituitrin and castor oil decreased the butter fat.—Physiol. Abst., **4**, 32.

(PITUITRIN) Sieben Jahre Hypophysenmedikation in der praktischen Geburtshülfe (Seven years therapeutic use of

hypophysin). Holfauer (J.), Monatschr. f. Geburtsh. u. Gynäk. (Berlin) 1918, **48,** 325.

An extended summary of the author's results from the use of hyophyseal extracts in medical practice. He concludes that the use of this substance has found a permanent place in medication.—F. S. H.

POLYGLANDULAR SYNDROME. Goldenberg. J. Cutan. Dis. inclu. Syph. (Chgo.), 1916, **34,** 387-88. Society transactions.

A man 28 years of age entered the hospital because of general malaise, headache, enlargement of the hands and feet and tumors of the face, trunk, and extremities. The Wassermann reaction was negative. The tumors were osseous, epidermal, and infiltrations of skin tissue. The thyroid isthmus was palpable. Marked gaping of the lambdoid and coronal sutures existed. The sella turcica was not enlarged, but the anterior and posterior clinoid processes were unusually thin. The condition was diagnosed as dyspituitarism and dysthyroidism. The patient was put on thyroid extract and the dosage increased up to 25 grains per day. Upon being discharged the dose was reduced to 1 grain a day. The tumors were reduced by one-half at the time of dismissal.—H. W.

SECRETIN, Is Vitamine identick met—? Jansen (B. C. P.), Geneesk. Tijdschr. ned. Indie, 1918, **58,** .....

The anti-beriberi vitamine from rice does not cause pancreatic secretion in the dog, hence is not identical with vitamine, as has been asserted. Physiol. Abst., **4,** 29.

SECRETIN, The question of the stability of—. Carlson (A J.), Kanter (A. E.) and Tumpowski (I.), J. Am. M. Assn. (Chgo.), 1918, **70,** 115-118.

Physiological tests of Beveridge's patent preparation of secretin show it to be inactivated by the gastric juice, without effect when given by the mouth, and having no greater stability in keeping qualities than the preparation of Bayliss and Starling. It should not be given intravenously since it contains split-protein products and living bacteria.—F. S. H.

(SEX) Studies on sex in the hermaphrodite mollusc Crepidula plana. III. Transference of the male-producing stimulus through sea-water. Gould (H. N.) Anat. Rec. (Phila.), 1919, **16,** 149.

The gastropod mollusc Crepidula plana passes through a male phase, a transitional phase, and a female phase during its life. The male phase is unstable and occurs only as the result of a stimulus furnished by an individual of the same species larger than the one stimulated. Complete isolation of small sexually undeveloped specimens over long periods shows that no development of male characters takes place under such conditions further than the formation of a few spermatogonia. In time female characters appear. Small sexually undeveloped individuals confined at fixed distances of from 4 to 7 mm. from large females, where contact is prevented, will in a majority of cases develop male characters to various degrees of maturity. Fewer and less well-developed males are produced under such conditions than when the small animals are nearer the source of stimulus. Large individuals of Crepidula fornicata, a species related to C. plana, have not been found to induce male development in small Crepidula plana except in a few doubtful cases. The stimulus to male development acts in such a manner as to indicate that it is a substance given off from the bodies of the large Crepidula plana, diffusible through seawater, but very unstable.—Author's Abst.

(SEX) The ineffectiveness of oxygen as a factor in causing male production in hydatina senta. Whitney (D. D.), J. Exp. Zool. (Phila.), 1919, **28**, 409-492.

Not of endocrine interest.—M. M. H.

SEX, The determination of—. Apert (E.), Med. Fortnightly (St. Joseph, Mo.), 1918, **1150**, 134-38.

Published elsewhere; abstracted Endocrin., 1919, **3**, 92.

(SEX GLANDS) Distrophia genito-glandular. Alves Mauricio (M.) Annaes da Policlinica Geral do Rio de Janeiro (Brazil), 1918, **3**, 363.

The author follows Aloysio de Castro and Souza's classification. Three brothers of the same family had all the characteristics of adiposo-genital dystrophy. Mauricio believes that the condition is hereditary. In case of the oldest the condition began at one month of age. The third had several fractures.

—G. P. G.

STERILITY. Gelser (G. M.), N. Y. State J. Med. (N. Y.), 1919, **19**, 174.

A general review of the causes of sterility. It is concluded that sterility is more frequently attributable to the male than the female.—H. W.

(THYROID) An experiment to increase the iodine in the thyroid. (Ein Versuch zur Anreicherung der Schildrüse an Jod. Strauss (E.), Ztschr. f. physiol. Chem. (Strassburg), 1919, **104,** 133.

It is possible to increase the amount of iodine in the thyroid of a dog when NaI is given. This has also been observed after extirpation of a lobe of the gland.—J. K.

(SYMPATHETIC N. S.) Acute changes occurring in the cells of the solar plexus in intestinal conditions. Myerson (A.) Boston Med. and Surg. J., 1919, **180,** 207.

Report of two cases in which acute intestinal conditions occurred associated with acute changes in the nerve cells of the solar plexus of the type described as acute Nissl degeneration. Case 1. A woman of middle age suffering suddenly died of volvulus. The cells of the solar plexus demonstrated acute axonal reaction, atrophy of nerve cells, marked pigmentation, complete disappearance of Nissl bodies, and peripheral placing of nuclei. In some cases the nucleus was completely extruded from the cell. Similar changes were not found elsewhere. Case 2. A juvenile paretic dying of pleurisy with effusion of tubercular origin demonstrated at autopsy fecal impaction and congestion of the peritoneal blood vessels. Histological preparations of the solar plexus tissue demonstrated axonal reaction in the sympathetic cells. Because of these findings the author thinks it likely that part of the collapse and shock noted in such cases as volvulus, intussusception, and acute intestinal obstruction of any type may be related to the changes in the nerve cells of the solar plexus.—H. W.

TESTES, Conservation in the management of trauma and diseases of the—. Lydston (G. F.), N. Y. Med. J., 1919, **109,** 800.

Before a tuberculous testis is sacrificed by total ablation a careful examination should be made to determine whether or not any healthy portion of the gland still remains. If so the apparently healthy portion should be resected, cutting as wide as possible of the infected area. Then, instead of replacing the gland tissue in the infected scrotum, it should be implanted in the rectus muscle in the suprapubic region beneath the superficial fascia. Even if very small, such auto-implants

preserve virility and, in addition, do their very important share in keeping the nervous functions and general nutrition at or near par.

Epididymotomy should be performed in all cases of epididymitis as a prophylactic measure against sterility from vas or epididymal occlusion or, perhaps, from infection. Small abscesses often develop very early in epididymitis, with later disastrous results not ascribed to the true cause, infection. In known or suspected malignant growths of the testicle, the highest degree of conservatism demands early and thorough operation. Hematomas of the testes demand opening and removal of the extravasated blood. Pressure is relieved and the testis is protected from subsequent damage by tissue and fluid constriction. The operative incision of the tunica albugina is indicated in orchitis secondary to mumps.—H. W.

TESTES, Cross-racial transplantation of—. Further report of case. Lydston (G. F.) J. Am. M. Assn. (Chgo.), 1919, **72**, 1614.

The testes were taken from a negro who had been hanged for murder and implanted in the scrotum of a white moron. After 5 months little atrophy of the organs was apparent and condition of the patient was much improved so that he was able to perform heavy labor.—R. G. H.

(TESTES) War edema and the testicular hormone (Kriegsoedem und endocrine Hodenfunction). Reach (F.) Wien. klin. Wchnschr, 1918, **31**, 1249.

Reach observed that many subjects with edema had atrophic testes or cryptorchism. In 26 cases in which no success was had with dietary treatment, testicular opotherapy was tried. In 14 cases the results were splendid, the patients being cured. In 12 cases no result whatever was obtained.—J. K.

(TESTIS) The sympathetic innervation of the testis in the dog. Kuntz (A.) Anat. Rec. (Phila.), 1919, **16**, 54.

The sympathetic nerve supply to the testis is derived from the third, fourth, fifth, and sixth lumbar segments of the sympathetic trunk. These fibers descend along the course of the spermatic artery and vein. The hypogastric nerve supplies some fibers to the pelvic end of the vas deferens; however, these fibers probably do not reach the testes. Sympathetic fibers are supplied to all structures in the spermatic cord and testis which contain smooth muscle. There is no evidence that sympathetic fibers terminate in relation either to interstitial cells

or spermatogenic elements. Section of the sympathetic nerves to the testis results in degeneration of the seminiferous tubules. —Author's Abst.

THYMUS, Enlargement of the—treated by the Roentgen ray. Friedlander (A.) Tr. Am. Pediat. Soc. (N. Y.), 1917, **29,** 77-85.

Published elsewhere. Abst. Endocr., **1,** 519.

(THYMUS ADRENALS) Relation of status thymo-lymphaticus to suicide in soldiers (Die Beziehungen des Status thymico-lymphaticus zum Selbstmord von Soldaten). Neste. Arch. f. Psych. (Berl.), 1919, **60,** 43.

Neste frequently found at post-mortem of soldiers who had committed suicide a hyperplasia of the thymus and lymph glands together with atrophy of the adrenals.—J. K.

(THYMUS ADRENALS) Sudden death (Plötzliche Todesfälle). Meyer (O.), Münch. med. Wchnschr., 1919, **66,** 261.

Two cases are described. In the first suffocation resulted from edema of the glottis following an anti-typhoid vaccination. Autopsy showed status thymo-lymphaticus. In the second sudden death occurred during simple faradisation. At post-mortem hypertrophy of the thymus and atrophy of the medulla of the adrenals was found.—J. K.

(THYMUS) Eine neue Funktion der Thymusdrüse nebst Bemerkungen uber anderweitige Beziehungen zwischen inneren Sekreten und Nervensystem. Asher (L.), Cor. Bl. f. Schweiz. Aerzt. (Basil), 1916, **46,** 1565-67.

The work of Basch and Matti shows that the thymus has an important influence on body growth. Asher states that his own investigation shows that intravenous injections of thymus extracts, if given properly, exert no harmful effect on the heart or circulation. Experiments in his own laboratory have shown that injections of thymus exert a definite counteracting effect on muscle fatigue. This result is not obtained by using other internal secretory glands, or pure nucleoprotein. It has not been determined whether this effect of the thymus is exerted centrally or peripherally.—E. N.

THYMUS and PARATHYROID, Further proof of the antagonism existing between the—. Uhlenhuth (E.), Proc. Soc. Exp. Biol. and Med. (N.Y.), 1919, **16,** 70.

The larvae of Amblystoma opacum have no parathyroids until metamorphosis occurs. Feeding thymus to them while in the larval state results, as previously reported, in tetanic convulsions. It was found, however, that after the development of parathyroids three animals were able to subsist for seven months on thymus gland without the appearance of tetany. —R. G. H.

(THYMUS) The persistent vivescence of the thymic function. Goffin (O. J.), Med. Sentinel (Portland, Ore.), 1918, **26,** 275.

The author noticed that in most cases of simple goitres in boys in Portland there were certain peculiarities common to all. They were tall for their age, spare of hair, had pale skin, round limbs, were rather feminine in feature, had hypertrophied tonsils, a rounding of the chest over the thymus and sometimes a greater than normal area of dullness over the region of the thymus. They were slow in developing. Goffin ascribes these symptoms to persistence of the thymus, and asserts that the deficiency of iodine in the thyroid has an influence on metabolism in the young, superinducing an abnormal persistent vivescence of the thymus. He believes in the old theory that the thymus has an antagonistic action on the gonads in their maturing at puberty. He advises iodized water or thyroid extract in the daily diet of children who show signs of development of hyperplasia of the thyroid. He does not attempt to prove his case by any detailed histories, X-ray reports or any other exact scientific data. Some would be slow to accept his statement that enlargement of the thymus would give much of a perceptible bulging of the sternum.—M. B. G.

(THYMUS) The role of the thymus gland in exophthalmic goitre. Eddy (N. B.), Can. M. Assn. J. (Toronto), 1919, **9,** 203-212.

In an attempt to determine whether an excess of the product of thymic activity in the circulating blood could cause exophthalmic goitre, subcutaneous injections of thymus gland substance were made into six rabbits for a period of eight weeks. Three received 5 mgm. per kilogram of body weight and three received 10 mgm. per kilogram for each dose. Forty injections were given to each rabbit. When compared with two control animals no evidence of the production of symptoms characteristic of exophthalmic goitre was discovered, (weight of thyroid glands, body weight, pulse rate, width of palpebral fissure). A review of the literature (largely clinical), however, seems to indicate the existence of some relation between the

thymus gland and exophthalmic goitre. The nature of the connection is not clear.—L. G. K.

(THYMUS, THYROID) A propos des corrélations fonctionnelles entre le thymus et le corps thyroide (The functional relations between the thymus and the thyroid glands). Dustin (A. P.) and Zunc (E.), J. Physiol. et Path. Gen. (Paris), 1918, **17,** 905-911.

From a study of the weights of the thymus and thyroid glands in normal men killed in war the authors show that if the weight of the latter is small the weight of the former tends to be great and inversely that a large thyroid accompanies a small thymus. There is, however, a much greater variation in the weights of the thyroid than in the weights of the thymus in different individuals. Extensively atrophied thymus glands are rare. The authors are of the opinion that atrophy of the thymus is greatly influenced by, or even depends upon, one or more thyroid hormones. This would explain the correspondence of a small thymus with a hyperfunctioning thyroid and also the inverse condition. On the assumption that the thymus regulates the distribution of the nucleoproteins and that those are necessary for cell division the authors suggest an explanation of the role of the thyroid gland in the development of the organism.—L. G. K.

(THYMUS) Two cases of sudden death associated with enlargement of the thymus, occurring in the same family. Brailsford (A.M.), J. South Carolina M. Assn. (Greenville), 1917, **13,** 447-449.

The sudden death of two children of four months is attributed to an enlarged thymus pressing on the trachea, since autopsy of one case showed the thymus completely covering all the structures of the superior and anterior mediastinum, extending from 2 cm. above the isthmus of the thyroid to 12 cm. below and closely hugging the trachea. The gland was 12 cm. long, 5 cm. wide and weighed 34 grams. No other abnormalities were found.—F. S. H.

(THYROID) A case of myxedema. Allen (M. B.) Southern Med. J. (Birmingham), 1919, **12,** 185-87.

A woman of 52 had slowly developed typical myxedema. Beginning with an attack of puerperal fever at 27, she had gradually lost strength and gained weight, reaching 89.5 Kg. (240 lbs.). She was physically incapacitated for any work and

was mentally depressed and irritable. Under thyroid treatment she lost 65 lbs. in 25 weeks and was restored to physical and mental normality. After some experimentation, 0.10 gm. thyroid extract t. i. d. was found to be for her case the proper dosage.—R. G. H.

(THYROID) Acute thyroiditis. Beilby (G. E.) Proc. Med. Soc. State N. Y., J. Am. M. Assn. (Chgo.), 1919, **72**, 1567.

In a series of ninety-one cases of various forms of thyroid lesion, in which an operation was performed, I have met with three instances of acute thyroiditis. In two of the cases, infection occurred in normal thyroid glands. The third case was an infection of a cystic adenoma of the thyroid. In two of the cases the infection was a direct extension from a laryngeal and tracheal infection. The infecting organism was a staphylococcus. The third case occurred during an attack of influenza and represented a hematogenous infection. Cultures in this case yielded a hemolytic streptococcus.—Quoted.

(THYROID) Algunas observaciones de bocios exoptalmicos tratados por inyectiones de agua caliente (Boiling water injections in exophthalmic goitre). Olivieri (E. M.) and Ronchi (P.) Prensa Med. Arg. (Bs. Aires), 1917-18, **4**, 285.

Published elsewhere. Abst. Endocrin. **2**, 207.

(THYROID, ADRENAL) Fatigue disease as exemplified in functional disorders of the stomach and thyroid gland. Rogers (J.) Arch. Int. Med. (Chgo.), 1919, **23**, 498.

From a thorough consideration of the physiology of fatigue and from experimental and clinical observations the author is led to believe that functional disturbance of the thyroid gland and the stomach is due to loss of balanced innervation to the parts; this loss results because of fatigue of the nerve endplates of the nerves supplying the organs. The etiology of hyperfunctionation of the stomach, with or without ulcer, should not be considered a "neurosis" or pathological condition of the vagus, but a defect or failure in functionation on the part of the gastric and possibly other parts of the sympathetic nervous system, including the adrenal glands. The ulcer should be considered a secondary or incidental lesion. If the normal action and quiescence of the stomach are dependent upon the integrity of the organ's double nerve supply in conjunction with the secretions or products of other viscera, then any interference with this relationship, as a fatigue failure of the gastric sympathetics, might be followed by a defect in nu-

trition which would be localized in the region of greatest anemia, or where the muscular contractions are most pronounced. Hence, gastric ulcers may be considered the result of trophic changes. Disturbances of the stomach should, therefore, be interpreted according to the functions of the involuntary nerves in relation to the balance found to exist between the vagus and sympathetics.

The functional disorders of the thyroid, like those of the stomach, are apparently of the same character and occur in the same type of "nervous" individuals. The exacerbations and remissions of these disturbances also occur under the same conditions of fatigue, and the symptoms and pathologic physiology in both organs are usually traceable to abnormal functionation of the involuntary nerves. The thyroid through its secretion apparently activates, not the inhibitory or sympathetic system, but all the functions which are dependent upon impulses discharged through the vagus or autonomic terminals. Fatigue of the sympathetic would then allow an unopposed action on the part of the vagus, which in turn would result in overactivity of the gland. The functional thyroid diseases apparently begin with a simple hypertrophy, which is accompanied by evidence of hyperthyroidism. Such conditions differ from the signs of fatigue only by the presence of goitre.

Observations upon thyroid feeding indicate that the patient to be benefited by such treatment must possess a certain minimal amount of functionating thyroid epithelium, otherwise the medication is useless or harmful. If the thyroid epithelium or its vagus nerve supply, or both, fail to functionate, thyroid feeding is useless. The author reports favorable results in the treatment of hyperthyroid cases by the administration of a few minims of an alcoholic or hydrolyzed extract of the thyroid, 1/100 or 1/50 of a grain of the dried nucleoprotein obtained by precipitating with 10 per cent acetic acid from a saline extract of the hashed fresh gland being used. From 1/20 to 1/4 grain doses every 3 or 4 hours of the commercial desiccated thyroid powder is less often satisfactory. In cases of manifest hyperthyroidism, the author concludes it to be reasonable therapeutics to attempt to reinforce the presumably weak or defective inhibitory or sympathetic system by feeding some derivitive of the adrenal gland. Epinephrine is clinically not as beneficial as an alcohol or hydrolyzed extract of the whole gland, as is the nucleoproteid material. That is, treatment is based upon the grounds that the vagus stimulates the thyroid to action while the sympathetics act to inhibit or check the vagus. Adrenal preparations also seem to have been used with good results in the treatment of "nervous" stomachs.—H. W.

(THYROID? ADRENIN) Leukocytic studies on soldiers with irritable hearts. Gay (L. N.) Arch. Int. Med. (Chgo.), 1919, **23,** 603.

A slight degree of leukocytosis is found in the "unclassified group" of soldiers with irritable heart. Patients of the type classed as "Constitutional Inferior" demonstrate a high leukocytic count; other types show normal counts. Patients with "irritable heart" show a relative lymphocytosis, the limits ranging between 15 and 51 per cent. A marked leukocytosis occurs in both patients and controls after the injection of epinephrin, 0.5 cc. of a 1:1000 solution. The increase is more marked in patients with positive reaction than in controls who did not respond to the drug. No greater variation occurs in the differential formulas after the injection of epinephrin than before. Morphological studies of the blood in cases of "irritable heart" show nothing of significance that might assist in the diagnosis of such cases.—H. W.

(THYROID) Blood sugar in hyperthyroidism. Dennis (W.) and Aub (J. C.), Arch Int. Med. (Chgo.), 1917, **20,** 964-972.

In a series of eighteen patients having hyperthyroidism the blood sugar was determined after a fourteen or fifteen hour fast and compared with that after the feeding of 100 gms. glucose in lemonade or "postum," 50 gms. bread, and 20 gms. butter. Hourly samples were taken over a period of three or four hours and the sugar content determined. It was found that fasting hyperglycemia is extremely rare, while alimentary hyperglycemia was observed in every case. No relation was observed between the degree of hyperglycemia and the glycosuria, nor was there any relationship between the severity of the intoxication and the occurrence of the hyperglycemia. After rest or operation the alimentary hyperglycemia was of a lower order. In two cases of hypothyroidism no change in fasting blood sugar level was observed to result from the administration of thyroid extract.—F. S. H.

THYROID, Carcinoma of lateral aberrant—. Wohl (M. G.) Interstate M. J. (St. Louis), 1917, **24,** 1044-49.

Clinical report of a case of adeno-carcinoma of an aberrant thyroid. Microscopic sections demonstrated a papillary adeno-carcinoma. An aberrant thyroid may be defined as normal or abnormal thyroid tissue, not connected directly with the thyroid gland, and occupying any position along the path of embryonal development of the gland.—H. W.

(THYROID) Causes and prognosis of exophthalmic goitre. Bram (I.), Arch. Diag. (N. Y.), 1919, **11,** 177.

Proper medical attention applied for the required length of time will, with few exceptions, cure every case of exophthalmic goitre. Pressure or malignancy of the thyroid should be the only indications for operation.—H. W.

THYROID. Clinical experience in 300 operations for goitre (Klinische Erfahungen bei 300 Kropfoperationen). Orth (O.), Deutsche Ztchr. f. Chir. (Leipzig), 1919, **148,** 360.

An article of great interest from a surgical point of view. Some cases of endocrine interest are described. A goitre occurred after extirpation of the spleen and in another case after operation for a myoma uteri. Some authors have observed an unfavorable result in pulmonary tuberculosis after the operation for goitre. The author did not observe this.—J. K.

(THYROID) Contribution a l'étude des goitres congénitaux chez les hérédo-syphilitiques. Pellegrini (R.), Arch. de med. exper. et d'anat Pathol. (Paris), 1916-17, **27,** 420-29.

A case report of a prematurely delivered foetus of 460 grams, the thyroid of which weighed 10 grams—the usual weight of this gland at birth being about 1.5 grams. The histological picture was parenchymatous goitre with alveolar exfoliation. Correlating this with reports of other investigators, and with the fact that both parents were syphilitic but non-goitrous the author concludes that congenital goitre may appear in the child as an effect of parental syphilis.

—F. S. H.

THYROID, Diet in diseases of the. Amesse (J. W.), Colorado Med. (Denver), 1919, **16,** 113-21.

On first examination it would appear that a discussion of the influence of diet in these obscure disorders must be purely theoretical. Intensive bio-chemical studies during the past decade, however, have developed many significant facts bearing on this problem. Reid Hunt has reported that there are items in the average ration which build up materials in the thyroid capable of combining with iodine or which increase the iodin receptors of the gland. Since the functions of the thyroid depend, in part, on the iodin content, a knowledge of the relative amounts of this important element in the common foodstuffs is desirable. Hunter and Simpson have called attention to the seasonal variation of the quantity of iodin found

in the thyroids of sheep subsisting at times on sea weed. During these periods the iodin content of their thyroids has been enormously increased. The influence of thyroid extract in goitre, Graves' disease, cretinism and myxedema is discussed. —Author's Abst. (abbreviated).

(THYROID) Disturbances in dental evolution in infantile myxedema (Troubles de l'evolution dentaire dans le myxedeme infantile. Superposition des deux dentitions). Lereboullet (M. P.) et Lang Landry, Mme., Rev. neurol. (Paris), 1917, **30,** 128.

Discussion with illustration of a case of double dentition in a boy of sixteen presenting a typical syndrome of infantile myxedema.—F. S. H.

(THYROID) Electrocardiographic observations in toxic goitre. Krumbhaar (E. B.) Tr. Assn. Am. Physicians (Phila.), 1917, **32,** 368-403.

Electrocardiographic studies were made of 51 cases of goitre, mostly of toxic type, in as many cases as possible both before and after surgical operation. In the 47 patients who were operated upon (ligation, partial excision, enucleation of adenomata) three deaths occurred, two without recognized premonitory signs; in the third a development of negative T waves might have served as adequate warning. In 43 per cent of the cases the electro-cardiograms were essentially normal. In 22 per cent preponderating hypertrophy of the right ventricle (or tendency thereto) was found; similar hypertrophy of the left ventricle in 22 per cent was noted. The former after operation tended to return to normal, but the latter showed either no change or an increased preponderance.

Cardiac arrythmia was found as follows: Sinus, 4 cases; ventricular extrasystoles, 3 cases; auricular fibrillation, 3 and flutter, 1 case; delayed conductivity, 2 cases. The T wave was unusually prominent in most cases, and materially diminished after operation in about half the cases. The pulse pressure was above normal in most cases and diminished after operation. Systolic pressure was high in the cases with left ventricular preponderance, but did not exceed 170 mm. Hg. In the early cases of toxic goitre the characteristic tachycardia was not accompanied by any signs of myocardial change detectable by the string galvanometer used.

Successful treatment, either medical or surgical, it is concluded, by removing the intoxication, improves the cardiac condition, as shown by occasional disappearance of arrythmia,

diminution in the size of the T wave and in the pulse pressure as well as by the general clinical condition.—R. G. H.

(THYROID) Etiology and Treatment of Exophthalmic Goitre. Bergh (C.) Norsk Magazin for Laegevidenskaben (Christiania), 1919, **80**, 217-52.

Bergh is convinced that the tonsils, nose or throat are often the primary source of the infection causing the thyroid derangement responsible for exophthalmic goitre. He has now a record of 11 cases in which treatment was directed to cure the pathologic conditions in nose and throat, and the exophthalmic goitre subsided. He cites further Salling's report on 97 cases of exophthalmic goitre in 13 of which the disease had followed immediately on an infectious sore throat, and he has found 42 on record of a similar briefly preceding infectious disease. In three of Salling's cases an acute infectious disease caused the flaring up of the apparently cured exophthalmic goitre, and in 20 others the exophthalmic goitre became much worse after an intercurrent acute infection. No less than 60 of the 97 displayed a tendency to infectious sore throat. In 62 of the 97 cases the exophthalmic goitre began evidently as a local process in the thyroid. These data sustain Bergh's asserficial, harmless thing, but may spread along the lymphatics to the thyroid. Migraine and cephalalgia have been frequently traceable to rhinopharyngitis, in his experience, and now he adds exophthalmic goitre to this group, and sustains his assertions that chronic catarrh of the nasal mucosa is not a supertions by the success of treatment of the rhinopharyngitis. As clinically normal conditions are restored in the nasal mucosa, the secondary affections subside. He treats the mucosa with massage, and commends the efficacy of this absolutely harmless treatment. It removes the chronic source of the infection, and the process in the thyroid then dies out. The outcome is better in the case of soft goitre. About thirty-five applications of massage were required in his cases, to never over forty-two.—J. Am. M. Assn., **72**, 1712.

(THYROID) Exaggerated fear of cachexia thyreopriva (de misplaatste vrees voor cachexia thyreopriva). Lanz (O.) Nederl. Tijdschr. v. Geneesk (Haarlem), 1919, **63**, 1086.

According to Lanz many physicians have an exaggerated fear of cachexia thyreopriva. Patients with Graves' disease who could probably be cured by an operation too often do not receive this because the doctors tell them it may result in their becoming idiots.—J. K.

(THYROID) Experimental lesions in the cervical sympathetic ganglia in relation to exophthalmic goitre. Wilson (L. B.) Tr. Assn. Am. Physicians (Phila.), 1917, **32**, 336-41.

Published elsewhere. See Abst. Endocrin., 1918, **2**, 530.

(THYROID) Exophthalmic goitre. MacKenzie (H.), Lancet (London), 1916, (2), 815.

A lengthy discussion of the etiology and symptomatology of exophthalmic goitre is offered. Briefly, his views on therapy are that the X-ray treatment may prove to be far the best means at our command. It must be supplied in no half-hearted way. It must be persevered with and in many cases continued for a long period of time. As for the surgical therapy, he sums up his views as follows: "If the operation is done at all, it should be performed under local anesthesia. Local anesthesia is especially indicated in younger subjects. Ligature of the thyroid arteries does not appear to have any appreciable effect on the disease and, therefore, if done at all, it should be the forerunner of thyroidectomy. Thyroidectomy does not cure unless a sufficient amount of the gland is removed. If possible, it is better to remove more than an entire lobe at one operation. The author does not think the risk will be appreciably increased if this is done. If a whole lobe is left behind, it is probable that another operation will be necessary at a later time, unless, by means of other treatment, a sufficient reduction of the remaining lobe can be brought about."—M. M. P.

(THYROID) Exophthalmic goitre. McGregor (J. K.), Can. M. Assn. J. (Toronto), 1919, **9**, 406-410.

A discussion of the methods of diagnosis and treatment of exophthalmic goitre. Contains no new data.—L. G. K.

(THYROID) Exophthalmic goitre in children. Welt-Kakels (Sarah), Arch. Pediat. (N. Y.), 1917, **34**, 529.

The writer reports a case in a boy 14 years of age. The interesting points were the presence of signs which are found in adults but not usually in children, such as tachycardia, Graef's sign, exophthalmos and tremor. The heart action was normal. The blood pressure was 135 to 140, which was unusual. The blood examination showed a red blood cell count of 3,300,000, a white cell count of 14,000 and hemoglobin of 58 per cent. This is not the characteristic picture in goitre, as there was a leucocytosis, whereas one would expect a lymphocytosis.—M. B. G.

(THYROID) Exophthalmic goitre, The surgery of—. Dunhill (T. P.), Lancet (London), 1917, **2,** 883-88.

A discussion of the views of various men regarding the surgical and medical treatment of exophthalmic goitre is offered. Dunhill sums up his views on the portion removed as follows: "I have always found that removal of one lobe and the isthmus gives improvement which is readily recognized by both patient and observer. The removal of rather more than half the remaining lobe almost always places a patient on a plane of health which enables her to work and play and to feel well whilst doing so. Occasionally a third operation is necessary. When necessary it is generally because one has not been able to judge how much was left at the second operation. The reason one is not able to judge is because the portion to be left is never dislodged." He presents two cases to show the degree of emaciation which may occur (photographs also shown) and how even in these cases an operation can be performed with reasonable safety, and with obvious improvement, when a sufficient amount of gland tissue has been removed. Two other cases are presented to show that the eyes may recede, if sufficient gland tissue is removed, even when the exophthalmos has been extreme. He reports two cases where a third operation was necessary to remove enough glandular tissue. The article is concluded with a brief discussion of the various views on the medical and surgical treatment of Graves' disease, and closes with the statement, that "there is no doubt that the degree of improvement following operation is much greater than that following X-ray treatment.

—M. M. P.

THYROID extirpation, Neuroretinitis (choked disk) sequel to—. Sherer (J. W.), Proc. Mo. State M. Assn., J. Am. M. Assn. (Chgo.), 1919, **72,** 1936.

A woman, aged 32, suffered severely with exophthalmic goitre. The thyroid gland was removed five years ago with complete recovery from all symptoms. For about five months she has been suffering severe asthenopic symptoms and during the last two months exophthalmos with swelling of the eyelids has developed. Pain through the left eye and the left side of the head is very severe. The fundus reveals the classic picture of neuroretinitis or choked disk. No hemorrhages occurred. Urinalysis and Wassermann are negative. The patient is nervous and emotional. The left eye has become totally blind during the last five days. The patient was put to bed on a restricted diet with bromids and alteratives. Pilocarpin

sweats were given regularly. Complete recovery ensued in two months. Exophthalmos and choked disk disappeared.—Official Abst.

(THYROID) Focal infection as a possible cause of exophthalmic goitre. Crouse (H.), Southwest Med. (El Paso), 1917, **1,** 9-11.

An editorial assigning focal infection as a contributing cause of exophthalmic goitre, based on the clinical care by the author of five cases each presenting the triad of symptoms of Basedow's disease. The difficulties disappeared after the removal of the markedly infected tonsils and the treatment of the patients with autogenous vaccines made therefrom.

—F. S. H.

(THYROID) Forma congestiva del hipotiroidismo. Mussio Fournier (J. C.), Rev. med. d. Uruguay (Montevideo), 1918, **21,** 155-63.

Published elsewhere. Abst., Endocrin., 1918, **2,** 199.

THYROID gland, Eczema in infants and the—. Ravitch (M L.) and Steinberg (S. A.), J. Cutan. Dis. (Chgo.), 1919, **37,** 312-16.

During an investigation of the cause of eczema in infants the author was impressed by the number of cases which occurred in breast-fed children. The great percent of cases were found in babies whose mothers demonstrated thyroid trouble either during pregnancy or lactation. The eczema in these cases was characterized by a dry, rough skin, perhaps moist, but never oily. The author believes that in all probability the milk of goiterous mothers causes a disturbance of thyroid function in the nursling. This disturbed gland in turn is not capable of maintaining a normal fat metabolism and the result is shown by the peculiar type of eczema found upon the child. Iodides should be administered when there is any sign of hypoactivity on the part of the thyroid either in the child or mother. Thyroid gland preparations should be given when the history or symptoms point to a myxedema. The daily dose of iodides should not be over 6 grains for adults. Infants should not receive over one grain a day.—H. W.

The THYROID gland. Its role in development and disease. Simonton (L. J.), N. Y. Med. J. (N. Y.), 1919, **108,** 281.

1. Hypothyroidism and hydrocephalus. Two sisters when

first seen showed diminished functional activity of the thyroid. Both had had marked goitre which had disappeared without treatment. The mother had a large goitre. The parents were first cousins. The first girl married a second cousin. She became pregnant and developed toxic vomiting; however, she carried her child to term. At nine years of age the child, a boy, wore a size 7½ hat. Although the lad's mentality was good, he was diagnosed as a hydrocephalic. The second girl married a non-relative and became pregnant. There was no vomiting, but she developed violent "heart attacks." Thyroprotein was administered with immediate relief. She was delivered at term of a child with a very large head. At four years of age the child wore a size 7⅜ hat. His mentality was normal. This case was also diagnosed as hydrocephalic. The history of these sisters bears out the known relationship between thyroid deficiency and consanguinity, and indicates a possible thyroid etiology of hydrocephalus.

2. Thyroid disease and sexual development in the female. The author states that practically half the female and some of the male population of the Cumberland Valley, Pa., suffer from goitre. The condition is due to thyroid dyscrasia, due either to limestone water, consanguinity or both. The interaction between the thyroid and ovaries has not been normal with a resulting subnormal sexual development. Most cases show frank hypothyroid symptoms: slow heart, irregularity of heart and menses, rough skin and scanty menstruation. Ninety per cent suffer from scanty, irregular menstruation. Correction of the hypothyroidism restored normal menstruation in all cases and also gave great relief from cardiac symptoms. In the sexually undeveloped cases—painful menstruation, irregularity, painful coitus, sterility, frigidity, etc.—corpus luteum obtained from the pregnant sow gave wonderful results. Lactation was established in several cases by the administration of thyroprotein (Beebe). Any attempt to discontinue the medication was followed by drying up of the milk.

3. Hyperthyroidism. Such cases were treated with tincture of iodine. In each instance (5 cases) the heart action became slower and in three the goitre completely disappeared. One exophthalmic case and one other with continued nervous symptoms were greatly relieved by thyroidectin medication

—H. W.

(THYROID) Goitre a metastases (metastatic goitre). Leclerc (G.) et Masson (P.) Bull. et mém. Soc. de Chir. de Paris,

1918, **44**, 1815. Abst. Surg. Gyn. & Obst. (Chgo.), 1919, **28**, 379.

In a man aged 67, a tumor had been noted for two years in the left costo-iliac region. It was removed and the man made a good recovery. From macroscopic appearance it was believed to be a sarcoma, but microscopically proved to be made up of thyroid tissue. The patient was then re-examined and a goitrous tumor found in the left sternomastoid region. It was painless. Some months later intense pain developed in the operated region and in the left thigh. Almost total paraplegia of the legs with incontinence of urine and feces followed and soon after, death. The author confidently ascribes the terminal phenomena to metastasis. Oseous tumors diagnosed sarcoma often prove to be typical colloid thyroid adenomata. The authors regard their case as of this type, histologically benign, but through multiple metastasis causing death. In the tumor in this case mitotic cell division was common, whereas in ordinary thyroid adenomata it is exceptional.—R. G. H.

(THYROID) Goitre and drinking water. (Krop en drink-water.) Kappenburg (B. D. G.) Inaugural Dissertation, Utrecht, 1919.

A large number of experiments on rats is reported. Little difference was found in the size of the thyroids in wild rats (mus decumanus) whether they had lived in places with no goitre or where it is prevalent. In Utrecht goitre is very frequently seen; in Sneek, a little town in the north of Holland, it is never observed. Rats in Sneek were given water from Utrecht to drink. No goitre resulted, nor any histological abnormalities. Similar animals kept under a comparable regime at Utrecht developed thyroids twice as large as normal; histologically they showed to greater or less degree the changes characteristic of goitre. Boiling the water did not prevent the thyroid enlargement. The author concludes that the role played by drinking water in the etiology of goitre is still problematic and that, in fact, it is not proved that it plays any part at all.—J. K.

(THYROID) Goitre, Exophthalmic—with special reference to etiology and Roentgen-ray treatment. Cole (W. A.), J. Med. Assn. Georgia (Augusta), 1918, **7**, 186-190.

The author considers the glandular and neurogenic theories of goiterous disturbances complementary. The X-ray treatment of twelve cases gave no absolute failures. The treatment was followed by reduction in pulse-rate, increase in

weight, and favorable response in diminution of insomnia, headache, and tremors. The thymus was simultaneously treated. The initial dose is small and followed after an interval of two weeks by the regular course of treatment. In all cases the dose was kept below the erythema stage. The doses were given every three or four weeks, lengthening the intervals between the treatments as the conditions improved, in this manner inhibiting the development of hypothyroidism, or cachexia strumipriva.—F. S. H.

(THYROID) Goitre in children. Peterson (E. W.), Arch. Pediat. (N. Y.), 1919, **34**, 526-29.

The writer reported a case in a girl first under observation at the age of five weeks. Her parents were Hungarian and gave a negative family history as to this condition. Labor had been easy and the child normal except for a relatively large tumor on the right side of the neck. The growth lay behind and to the inner side of the sternomastoid, extending from the level of the jaw nearly to the clavicle. It was made up of two masses, the larger situated above, smooth on the surface, of firm consistency and not fluctuating at any point. Below and to the side there was a distinct palpable nodulation. There was some difficulty in breathing for the first two hours, after which there was neither dyspnea nor dysphagia. The tumor was removed and found to be an adenoma with colloid degeneration of the thyroid. Nine days after the operation, the child had a convulsion, which was followed by frequent repetitions. Believing that the entire thyroid had been removed, thyroid extract was given and the tetany stopped. Thyroid administration was kept up for four years and then discontinued. A close watch on the girl since then has failed to demonstrate any symptom of hypothyroidism. Her physical and mental development has been normal.—M. B. G.

(THYROID) Goitre, use and misuse of treatment. Grimes (E.), J. Iowa State M. Soc. (Des Moines), 1917, **7**, 407-409.

The diagnosis of simple hyperplastic goitre must be accurate or else treatment will be disappointing or disastrous. It must be known whether or not the condition is cystic, parenchymatous, or interstitial, and whether accompanied by tuberculosis, or whether the case is one of hyperthyroidism. The external use of iodine is valueless and the internal administration of this drug is favorable in but a few cases, being distinctly harmful in cystic and parenchymatous types. X-ray

treatment is considered dangerous and surgical interference is advocated.—F. S. H.

(THYROID) Goitre, surgical vs. medical treatment. Smith (E. V.) Wisconsin M. J. (Milwaukee), 1918, **16,** 388.

Goitres are classified in three groups, i.e., Exophthalmic, toxic adenomata, and colloid. The treatment of exophathalmic goitre is primarily medical. Surgery should be considered only when it becomes absolutely necessary to relieve the patient. The medical treatment should consist of absolute rest, ice bags over the heart and a diet as protein-free as possible. Patients at the height of an attack should always be treated by non-operative measures until the severity of intoxication has begun to subside. There are two types of symptoms in toxic adenomata, one indicating chronic poisoning, the other pressure. The latter condition should, of course, be treated surgically. Cases of chronic poisoning should be given medical treatment for three weeks before operating. Patients so treated seem to withstand surgical procedures to a remarkable degree. Goitres of puberty respond well to the internal and external administration of iodides. Less surgery and more nonoperative care seems highly advisable in the handling of this type of goitre.
—H. W.

(THYROID) Goitre, differential diagnosis of forms of—. Pember (J. F.) and Nuzen (T. W.) Wisconsin M. J. (Milwaukee), 1918, **16,** 392.

A general review of the findings in various types of goitre. The authors consider the pathology found in enlarged thyroids to be more or less secondary to infection or some profound disturbance of the central nervous system which calls for an increased thyroid output. The latter, in turn, produces changes in the sympathetic nervous system, adrenals, and other organs. The combined effects of all these changes make up the picture of exophthalmic goitre, and the varying degrees of hyperthyroidism. Differential diagnosis is not considered difficult save in border-line cases of thyrotoxic goitres which are so often confused with enlargement of the thyroid due to the influence of infection, particularly to incipient tuberculosis, and neurasthenia.—H. W.

THYROID, Hemi-aplasia of the (Hemiaplasie der Schildrüse.) Dubs (J.), Zentralbl. f. Chir. (Leipzig), 1918, **45,** 401.

Aplasia of one lobe of the thyroid is very rare. The author describes 4 cases, controlled by operation. In these cases

the anomaly is congenital. The author describes one case with aplasia of the isthmus. These conditions have a practical significance in the operation for goitre or Graves' disease.—J. K.

(THYROID) Heredity of Graves' disease (Über dominant geschlechtsbegenzte Verurbung und die Erblichkeit der Basedow Diathese). Lenz (F.), Arch. f. Rassen und Gesellschafts Biologie (Leipzig and Berlin), 1919, **13**, 1.

A general discussion embodying no new data.—J. K.

THYROID. Hyperthyroidism: A clinical study. Boggess (W. F.), Kentucky Med. J. (Bowling Green), 1919, **17**, 157.

There is a rather close relationship between chronically infected tonsils and enlargement of the thyroid gland with thyro-toxicosis. Three cases of well defined Graves' disease in women between 20 and 30 years of age, with bad tonsils, recovered completely following removal of the tonsils. In atypical cases of Graves' disease, cleaning the crypts and relieving the infection of the tonsils and post-nasal spaces often brings about improvement in health with the abatement or amelioration of the cardio-vascular symptoms. The old etiological factors of fright, extreme emotional excitement or psychical trauma, and iodine therapy and iodine retention may suddenly precipitate the syndrome of hyperthyroidism, yet they in themselves should not be considered causative factors of the disease. The proper treatment of thyro-toxicosis is not the treatment of the heart or any one particular symptom, but the treatment of the condition in its entirety. The source of infection should be sought and removed. Rest, forced feeding, thorough alkalinization and the free use of iron and arsenic should be encouraged as therapeutic measures. The beneficial result sometimes seen following the use of thyroid extract is due to some favorable action in stimulating antagonistic glands, or in producing antibodies. But three cases, however, are definitely reported in which removal of focal infections brought about a cessation of thyroid symptoms. Nothing is said about possible cases who did not suffer from focal infections.—H. W.

(THYROID) Hyperthyroidism as occurring in sailors. Findlay (G. M.), J. Roy. Nav. Serv. (Lond.), 1917, **3**, 205-209.

Four men who had been subjected to the continuous strain of naval warfare developed typical symptoms of hyperthyroidism. They were given 5 gs. thyroid extract three times a day and the reaction compared with four other patients similarly

treated, but having shown no tendencies towards hyperthyroidism. In the four suspected cases the administration of the thyroid extract caused a marked exacerbation of the symptoms, while the controls were unaffected. Apparently these were cases where the original stimulus was psychological of fear or anger, excessive in character and affecting the most susceptible endocrine gland with subsequent development of characteristic symptoms of hyperthyroidism.—F. S. H.

(THYROID) Intralaryngeal struma. Dorn (J.), Beitr. z. klin. Chir. (Tübingen), 1919, **115**, 101.

A simple goitre without symptoms of malignant degeneration was penetrated through the right ligamentum crico-thyroideum and removed surgically. Later a metastasis appeared in the larynx. The successful removal of this was accomplished.—J. K.

(THYROID) Hyperthermie thyro-endocrinienne (Thyro-endocrine hyperthermia). Léopold-Lévi, C. R. Soc. de Biol. (Paris), 1919, **82**, 344-346.

Thyroid hyperthermia is classified under the following groups:

1. The subject is always too hot and sometimes presents a true thermophobia.
2. The sensation of heat is localized and is either continuous or intermittent.
3. It is not uncommon for the subject to have the sensation of fever, either localized or general. But the temperature is hardly above 37° C.; sometimes it is below normal.
4. Fever possible in mild endocrine cases.
   - **a.** The temperature regularly a few tenths of a degree above normal.
   - **b.** It may exist as a mild sub-febrile state, being exaggerated by any accessory factor (fatigue, emotion, menstruation).
   - **c.** Hyperthermia intermittently affects the course of the fever; there may be a periodic migraine accompanied by a rise of temperature.
   - **d.** Prolonged fever with remissions.

   Hyperthermia is accompanied by sweating, circulatory disturbance, thirst and disturbance of sensibility.

The relations between endocrine disturbance and hyperthermia are pointed out.

1. **Thyroid.** The author mentions the work of others in which an increased temperature was produced by giv-

ing thyroid. In his own experience he has observed hyperthermia resulting from an overdose of thyroid substance. In cases of hypothermia attending myxoedema, thyroid treatment frequently produced hyperthermia.

2. **Ovary.** As a result of the relationship of the ovary to the thyroid, during the menopause there is a hyperthyroid reaction and a consequent hyperthermia.
3. **Adrenal.** Hyperthermia from adrenal hyperactivity depends upon the concomitant hyperthyroidism.

The stimulation of metabolism plays an unimportant part in the mechanism of hyperthyroid hyperthermia. There is no appreciable modification of the urine in Basedow's disease. But it is accounted for by hyperactivity of the muscular system, with the manifest spasms and trembling, also by an overstimulation of the thermic centers already sensitized.—F. A. H.

(THYROID, HYPOPHYSIS) The relation of the pituitary and thyroid glands of Bufo and Rana to iodine and metamorphosis. Allen (B. M.), Anat. Rec. (Phila.), 1919, **16**, 137.

Administration of iodine mixed with flour brings about precocious metamorphosis in Bufo tadpoles from which the pituitary gland has been removed. This is accompanied by a marked shrinkage of the body. Iodine has no effect upon the changed color produced by the removal of the pituitary gland. In these operated tadpoles, the absence of the pituitary gland normally results in scanty deposition of colloid in the thyroid gland. Iodine feeding does not cause any marked increase in colloid deposition in the thyroid glands of these pituitaryless tadpoles. Great progress toward metamorphosis was produced by feeding iodine to Bufo and Rana tadpoles from which both the pituitary and thyroid glands had been removed. There is every evidence that complete metamorphosis would have been attained if the tadpoles had lived.—Author's Abst.

THYROID, HYOPHYSIS and PINEAL glands of Rana sylvatica, Experiments with the—. Hoskins (E. R. and Margaret M.), Anat. Rec. (Phila.), 1919, **16**, 151.

A. Thyroid. In 105 young larvae the thyroid fundament was cut to pieces but left in situ, and an additional thyroid fundament transplanted into the animal. Some of the larvae developed accessory thyroids, but this had no effect except perhaps in a few larvae that metamorphosed while small. The time of metamorphosis was not hastened. B. Hypophysis. The hypophyseal fundament was removed from 116 young

larvae after the method of Smith and of Allen, with the usual results in most cases. A few larvae became black. Some of these black larvae metamorphosed, but one did not, although it grew much larger than normal. Transplantations of the hypophyseal fundament into 62 young larvae gave negative results, although some of the transplants grew. C. Pineal. The pineal was removed from 70 young larvae, but regenerated either partially or completely and the larvae grew normally. The fundament of the pineal was transplanted into 19 young larvae. It failed to grow. D. Some of the larvae of the thyroid and hypophysis operations developed small accessory mouth-parts. These were mostly ectodermal outpouchings, but in some of them muscle fibers developed. One of these opened into the oral cavity.—E. R. H.

The THYROID in gynecology. Hayd (H. E.) Tr. Am. Assn. Obst. & Gyn., 1917, p. 165-171.

See Endocrin., **2**, 534.

(THYROID) Instabilité thermique a mécanisme neuro-thyroidien. (Thermic instability in the neuro-thyroid mechanism). Léopold-Lévi. C. R. Soc. de Biol. (Paris), 1919, **82**, 346-348.

Amongst numerous cases of thermic instability in mild thyro-endocrine states there are some in which both hypothermia and hyperthermia existed in the same subject. He separates these into two groups:

1. Hypothermia and hyperthermia succeed one another. The two phases may be of long or short duration. 2. Hypothermia and hyperthermia occur simultaneously. One part of the body may seem cold while another part is hot. It is considered that variations in the thyroid secretion act through the nervous system, causing thermic instability.—F. A. H.

(THYROID) La colesterinemia en la insuficiencia tiroidea (The blood content of cholesterin in thyroid insufficiency). Martinez (B. D.), Primer Congreso Nacional de Medicina (Bs. Aires), 1916, **4**, 24.

See Endocrin., **1**, 357.

(THYROID) Medical treatment of Graves' disease. Therap. Gaz. (Detroit), 1918, **34**, 390-96.

See Endocrin., **3**, 117.

(THYROID) Multiple Strumametastasen. Thomsen. Beitr. z. klin Chir. (Tübingen), 1919, **115**, 113.

An interesting case is described in which a goitre at operation showed under the microscope no sign of malignant growth. After operation, however, metastases occurred in bones, skin, mucous membrane and heart.—J. K.

(THYROID) Névroses et opotherapy. Blanc (J.), Prog. Méd. (Paris), 1917, **32**, 95-98.

In four cases of dysthyroidism resulting in psycho-thyroid disturbances, due to the war, with positive and exaggerated oculo-cardiac reflexes, the administration of powdered thyroid, iodothyroidin or thyroid extract, in doses of from 0.002 mg. to 1 mg. a day produced a favorable reaction and disappearance of the symptoms as evidenced by the diminution of the oculo-cardiac reflex.—F. S. H.

THYROID. Nervous cretinism. Crookshank (F. G.), Lancet (London), 1917, **2**, 604.

Crookshank has had 10 or 12 cases of nervous cretinism (corresponding to the cases that McCarrison described in The Lancet, 1908, ii, 1278) with various nervous manifestations, particularly spastic diplegia. His conclusions were: "In almost every case that I have seen which appears to deserve the appellation of 'nervous cretinism' there has been evidence of dysthyreosis in the mother or other members of the family. They go through various nervous phenomena, the more severe showing mental defects which are obvious from the earlier days, and the early appearance of spasm with nystagmus leads to the confident diagnosis of congenital spastic diplegia. Cases which have fallen in the latter class have responded well to thyroid therapy.—M. M. P.

(THYROID) Non-surgical treatment of exophthalmic goitre. Bram (I.), N. Y. Med. J. (N. Y.), 1918, **108**, 942-44; South. Clinic (Richmond), **41**, 225-35.

Hyperthyroidism is not a surgical entity, but is a disease which belongs to the internist, for the following reasons. Recent researches prove that Graves' disease is not a local condition, nor has it a local etiology. Though surgeons report very favorable surgical recoveries, clinical recoveries are rare, and in a vast majority of cases there is a postoperative return, occasionally with augmented vehemence, of all the signs and symptoms of hyperthyroidism. The patient who has been op-

erated upon, and who does recover clinically, gets well because of a carefully outlined system of postoperative non-surgical treatment or because of the fact that the case in question is one of those instances of spontaneous recovery and would have terminated favorably in spite of treatment. Internists who specialize in thyroid gland treatment cure more than 75 per cent of their cases of hyperthyroidism by dietetic, hygienic, medical, and electrotherapeutic measures.—H. W.

(THYROID) Observations on thyroidless Rana sylvatica larvae kept through the second season of normal metamorphosis. Hoskins (E. R. and Margaret M.). Anat. Rec. (Phila.), 1919, **16**, 152.

The larvae reached nearly their maximum size the first summer (66 mm.), but grew again slightly during the winter and more during the second spring and summer (72 mm.). They became relatively longtailed, the legs grew ½ mm., the head and back flattened, and the eyes became relatively far apart. The brain acquired a shape practically mature, but at a size much larger than normal, and the liver became nearly mature in shape. The hypophysis became relatively very large, especially the inferior lobe, and this lobe showed an increase in the relative number of eosinophilic cells. The anterior and superior lobes showed little structural differentiation. The thymus glands persisted and became relatively and actually large. They retained the larval shape and structure. The epitheloid bodies (parathyroids) became relatively large. The spleen became large, but was roughly proportional to the size of the larva. The kidneys enlarged both actually and relatively. The internal gills persisted and the lungs became large and functional. The intestines grew long and remained larval in type. The ovaries became large and large oöcytes developed. Maturation was not seen and oviducts did not develop, so the animals were not sexually mature. The testes became mature and formed spermatozoa which escaped into the kidneys. By successive extirpations of the end of its tail, a larva was made to regenerate 38.5 mm. of tail. It regenerated one small hind leg once, but not a second time after the regenerated leg was removed. The amount of time required for regeneration of the tail gradually increased. A thyroidless larva placed in a moist chamber lived two days, its volume decreasing 18 per cent, its tail shrinking 24 per cent in length, and its intestine contracting to about one-half the normal size, but not shortening perceptibly.—E. R. H.

(THYROID, HYPOPHYSIS, ADRENALS) A contribution to the study of vasomotor reflexes. Ogata (O.) and Vincent (S.), J. Comp. Neurol. (Phila.), 1919, **30,** 355-394.

This paper contains but a short section on the effect produced on the vasomotor reflexes by the injection of extracts of the ductless glands, or by extirpation of the glands. Injection of pituitrin or thyroidin (Parke, Davis & Co.) and extirpation of both thyroid glands show no significant results. Injection of adrenin ("adrenalin," Parke, Davis & Co.) seems to give a slight decrease of the pressor reflex. Tying off the suprarenals gives no clear results when the nerves of the limb are intact. The results in the denervated limb are discussed in a a paper in Endocrinology, 1919, **3,** 121-36. The experiments were made upon dogs.—M. M. H.

(THYROID) Pregnancy in a case of improved sporadic cretinism. Welz (W. E.), Am. J. Obst. (York, Pa.), 1919, **79,** 655-56.

Report of a case of contracted pelvis due to sporadic cretinism. The patient carried a fetus to term and was then delivered of a 7¼-pound child by Caesarean section. The child was placed upon a milk formula the fifth day because of failure of the mother to establish lactation. The mother made an uneventful recovery and left the hospital on the 14th day.
—H. W.

(THYROID) Radium therapy in hyperthyroidism. Aikins (W. H. B.), Internat. J. Surg. (N. Y.), 1918, **31,** 217-24; Boston M. & S. J., 1918, **179,** 558-64.

Published elsewhere. Abst., Endocrin., 1918, **2,** 537.

THYROID, Sarcoma of the (Primäre Sarkoma der Schilddrüse mit seltenen Metastasen). Kregliger, Arch. f. klin. Chir. (Berlin), 1919, **111,** 545.

Description of a case in which the clinical diagnosis was tumor of the stomach or liver. At the post-mortem examination a large sarcoma of the right lobe of the thyroid was found. There were metastases in the left lobe, the skin, the stomach, the peritoneum, both lungs, the heart, the bile ducts and the bladder.—J. K.

(THYROID) Scleroderma and sclerodactyly: report of a case, with Roentgen rays and review of the literature. Atwater (R. M.), Am. J. Med. Sc. (Phila.), 1919, **158,** 29-35.

A striking case is described at length. It is of endocrine interest in that, on a basis of possible thyroid etiology, the patient was given a two months' course of treatment with thyroid extract. From 0.065 to 0.13 gms. was taken three times daily; this dosage was subsequently somewhat reduced. The treatment appeared to be of no use and possibly even aggravated the symptoms.—R. G. H.

(THYROID) Some remarks on hyperthyroidism. Kuh (S.), Ill. M. J. (Chgo.), 1919, **35**, 190-92.

The fact that thyroid disease—particularly the inconspicuous forms—is more prevalent than usually recognized is emphasized. Slight degrees of "hyperthyroidism" are seen in individuals of splendid physique who are unconscious of any illness. The most important misleading complications are gastro-intestinal. The thyroid disorders often date back unrecognized to the time of puberty, as can often be determined by the examination of the family photograph collection. In women in whom diagnosis is difficult, advantage should be taken of the fact that the symptoms are often aggravated during menstruation. The author regards infrequent blinking as one of the most significant symptoms of Graves' disease; the occurrence of this seems not to be widely recognized. Excellent therapeutic results have been obtained in a large number of cases from the use of serum of thyroidectomized animals, fully 90 per cent of the patients reacting favorably. Doses of 50-60 drops three times daily should be used rather than 15 drops as recommended by Moebius.—R. G. H.

THYROID, Surgery of the—. Judd (E. S.), J. Iowa State Med. Soc. (Des Moines), 1917, **7**, 405-407; St. Paul M. J., **19**, 70-75.

In thyroidectomy Judd advocates leaving a small bit of the gland intact as well as the posterior capsule containing the parathyroids. With this procedure any tetany that may develop is of slight degree and easily controlled by the use of calcium lactate. The removal of all goitres presenting toxic symptoms is indicated.—F. S. H.

(THYROID) Surgical treatment of goitre. Webb (C. W.), Clifton Med. Bull. (Clifton Springs), 1918, ..., 12-18.

Published elsewhere. Abst., Endocrin. 1919, **3**, 115.

(THYROID) Surgical treatment of Graves' disease (Operative Behandlung der Morbus Basedowi). Fabian (E.), Beitr. z. klin. Chir. (Tubingen), 1919, **115**, 1.

A long, technical discussion of the subject embodying no new data.—J. K.

(THYROID SYMPATHETIC N. S.) The pathological changes in the sympathetic system in goitre. Wilson (L. B.), Am. J. Med. Sc. (Phila.), 1916, **152**, 799-812.

For abstract of a later report on this work, see Endocrin., 1918, **2**, 530.

(THYROID) The heart in myxedema (das Myxoedemherz). Ausmann (H.) Münch. med. Wchnschr., 1919, **66**, 9.

In myxedema dilatation of the heart may be observed. It is not influenced by digitalis, but is promptly cured by thyroid administration. An illustrative case is described.—J. K.

(THYROID) The influence of amines on the nitrogen metabolism in the dog without a thyroid (Beitrage zur Kenntniss der physiologischen Wirkung der proteinogen Aminewirkung auf der Stickstoff-Stoffwechsel schildrüsenloser Hundes). Abelin (J.), Biochem. Ztschr. (Berlin), 1919, **93**, 128.

The influence of phenylethylamine and para-oxyphenylethylamine on the nitogen metabolism of the dog without a thyroid was examined. The excretion of nitrogen is increased, diuresis occurs and the animal loses weight. These amines derived from protein have the same action as does the administration of the thyroid gland itself. This points to the fact that the amines have a great biological interest. It is probable that the active principles of the thyroid are not the proteins but the amines derived from them.—J. K.

(THYROID) The medical treatment of Graves' disease. Gordinier (H. C.), Dominion M. Monthly (Toronto), 1918, **51**, 49-59; Therap. Gaz. (Detroit), 1918, **24**, 390-96.

Published elsewhere; abstracted Endocrin., 1919, **3**, 117.

(THYROID) The medical treatment of exophthalmic goitre. Rice (J. F.), Med. Press (Lond.), 1918, n. s. **106**, 236-38.

Published elsewhere; abstracted Endocrin., 1919, **3**, 103.

(THYROID) The prevention of simple goitre in man. Kimball (O. P.) and Marine (D), Arch. Int. Med. (Chgo.), 1918, **22**, 41-44.

Published elsewhere. Abst., Endocrin., 1918, **2**, 204.

(THYROID) The value and limitation of radiotherapy in internal medicine. Boggs (R. H.), Med. Fortnightly (St. Joseph), 1918, **50**, 55.

Simple goitres are greatly benefited by radiotherapy. Cases of exophthalmic goiter should be handled carefully because the thyroid may be entering a period of hypofunction while other structures of the body show apparent effects of hyperthyroidism. Radium gives results comparable to those of radiotherapy. One may easily follow the effects of the rays by noting a reduction in pulse rate and an increase in body weight. The patients improve rapidly. An increase in weight was noted in 50 per cent of the cases and a reduction of the goitre in two-thirds. Radiotherapy has proven notably satisfying in the management of adolescent goitres.—H. W.

(THYROID) Tratamiento de bocio por injectiones de agua herviendo. (Goitre treated with boiling water). Ceballos (A.) and Bacigalupo (G.) Prensa med. Argent. (Bs. Aires), 1917-18, **4**, 285.

Published elsewhere. Abst. Endocrin., **1**, 536.

(THYROID) Treatment of 1000 cases of goitre (1000 Kropfkranke aus der Garre'schen Klinik). Naegeli (T). Beitr. z. klin. Chir. (Tübingen), 1919, **115**, 69.

A general discussion of the topic bringing forward no new observations.—J. K.

(THYROID) Two cases of myxedema. Leonard (E. F.) Interstate M. J. (St. Louis), 1917, **24**, 1171-74.

Case 1. Myxedema which developed the syndrome of exophthalmic goitre while under thyroid medication. Withdrawal of the thyroid treatment, rest and tonics resulted in a return nearly to normal.

Case II. A patient suffering from myxedema with intoxication symptoms recovered under thyroid treatment.—H. W.

THYROID. Two cases showing the effect of the incidence of English measles upon pre-existing Graves' disease. Jennings (H. C.), Lancet (London), 1918 (i), 906.

The writer reports two cases of measles occurring in patients with a pre-existing Graves' disease. In one, there were rather marked symptoms of Graves' and the patient died during the course of measles. In the other, the symptoms of

Graves' were milder, but the attack of measles aggravated the condition so that four weeks later surgical intervention was necessary.—M. M. P.

(THYROID) Tracheomalacia and goitre (Tracheomalazie und Struma). Denk (W.) and Hofer (G.), Arch. f. klin. Chir. (Berlin), 1918, **110,** 401.

From 1901 to 1917 in one clinic in Vienna 1967 patients were operated upon for simple goitre. In 8 of these it was necessary to perform tracheotomy because of asphyxia. Four of these cases showed the classical anatomical picture of tracheomalacia. The authors record 3 other cases not from this clinic.—J. K.

(THYROID) Thyreoidea und Menstruation. Weidenmann (M.) Ztschr. f. Geburtsch. u. Gynäk. (Stuttgart), 1918, **80,** 419.

The author observed that the thyroid increases from one to two cm. in size at menstruation, the increase beginning in the premenstrual period one or two days before and reaching its maximum growth on the first day of menstruation. With the cessation of the period the thyroid regains its original size. In the interval between two periods other smaller changes occur which may be attributed to ovulation.—F. S. H.

(THYROID) Uber die Ossifikationsstörungen beim endemischen Kretinismus und Kropf. Wegelin (C.), Cor. Bl. f. Schweiz. Aerzt. (Basil), 1915, **46,** 609-25.

It is generally accepted that lessened function of the thyroid inhibits, while increased function promotes, skeletal growth. The history of the early work on myxedema and other hypothyroid conditions is reviewed by Wegelin. Cases of myxedema occurring spontaneously in children are due either to complete absence or rudimentary development of the thyroid. Complete absence in such cases has been, up to the present, demonstrated in only eight cases. In other cases of so-called "athyreosis" aberrant thyroid tissue is present in the region of the ductus thyreo-glossus, most frequently at the base of the tongue. Such individuals may develop normally, symptoms of cachexia thyreopriva appearing only after operative removal of the thyroid tissue. In other instances, hypothyreosis is present from the beginning. Individuals with aplasia or hypoplasia of the thyroid exhibit a well marked dwarfism and even when in mature years are short. The

oldest patient of this group—that of Bourneville—was thirty-seven years old, and measured 100 cm. Hanan and Steinlin have shown that in the thyroidectomized animal fracture healing is slower than in normal animals. On the contrary, observations have been made indicating that skeletal growth is promoted by hyperthyreosis. The relation between the thyroid function and certain disturbances of growth is not so clear. This is especially true of dwarfism in endemic cretinism. Some authors are inclined to believe that the dwarfism is not due to the hypothyroid condition, but rather that it is only a parallel symptom of the same underlying cause. Wegelin made a careful study of this subject in seventy new born infants who came to autopsy at the Pathological Institute of Bern, which is a centre of endemic cretinism. The strikingly frequent absence of ossification centres in these new born babies he states is apparently an expression of an inhibitory influence which is widely scattered in that region. Only six babies had normal sized thyroids, weighing from one to three grams. The others were enlarged, there being many over ten grams, two weighing twenty grams, while one reached the enormous weight of thirty-nine grams. In the six cases with normal thyroids, there was only one with absent ossification centres. All the cases without ossification centres showed enlarged thyroids, although many showing normal ossification possessed a more or less large struma. Skeletal inhibition and the size of the thyroid, therefore, are not exactly parallel, for the function of the thyroid does not, of course, go hand in hand with its size. Wegelin concludes that in those regions where goitre is endemic it is common to see marked inhibition of bony development during the foetal period and that the probable cause of this inhibition is hypothyroidism.—E. N.

(THYROID) The use of electricity in the various forms of goitre. Myers (E.) Northwest Med. (Seattle), 1916, **15**, 11.

Recommends strongly the treatment of hypothyroidism accompanied by simple goitre by cataphoresis. Other types are not so amenable to this treatment.—J. P. S.

(THYROID) Toxic goitre in a girl ten years old. Sawyer (A. W.) Ann. of Surg. (Phila.), 1916, **64**, 371.-75.

Report of a case which, except as to the age of the patient, was not unusual.

THYROID, Traumatic lesions of the—and their surgical treatment (Lésions traumatiques du corps thyroïde et leur traite-

ment chirurgical). Alamartine (H.) Presse Méd. (Paris), 1919, ..., 107-8.

Of technical surgical interest. Three cases are discussed. —R. G. H.

(THYROID) Tuberculose et goitre exophthalmique. Creyx, J. de Méd. de Bordeaux, 1918, **89,** 314-16.

A case of exophthalmic goitre concurrent with pulmonary tuberculosis is described briefly, but discussed theoretically at some length.—R. G. H.

(THYROID) Zur Lehre vom Oedem (Theory of Edema). Klemensiewicz (R.) Archiv. f. Psych. (Berlin), 1918, **59,** 842.

The author has carried out experiments on edema, ligating the blood vessels of the rabbit's ear. It was found that edema is due not to a swelling of the tissue elements, but to accumulation of fluid in the intercellular spaces. Even though the edema has an immediate mechanical cause, the influence of diminished function of the thyroid cannot be denied. The best remedy is thyroid extract.—J. K.

THYROIDECTOMY, The technique of—. Warnshuis (F. C.) Nurse (Jamestown, N. Y.), 1916, 247-56.

An illustrated account; elementary.—R. G. H.

(TONUS) Sympathetic tonus, vagotonus and hyperthyroidism. Troell (A.) Allmänna Svenska lakaretidningen (Stockholm), 1916, **13,** 137-159.

Later published in English. See Endocrin., 1918, **2,** 545.

UTERUS, The undeveloped—. Bonfield (C. L.), N. Y. State J. Med. (N.Y.), 1919, **19,** 40.

Rudimentary and infantile uteri are rare and are usually found associated with development anomalies of the vagina. On the other hand the pubescent uterus is comparatively common. The size varies from that which is almost infantile in its dimensions to that which is almost normal. The majority are sharply anteflexed, but an occasional one is equally sharply retroflexed. There is frequently a coincident lack of development of the ovaries which are prone to undergo cystic degeneration while the woman is still young. Menstruation is late in being established and early in ceasing, making its first appear-

ance at about 17 and its last before 40. Although the condition makes itself manifest with the approach of puberty the majority of sufferers do not seek medical attention until 19 to 24 years of age. Sufferers from pubescent uterus may be classed in three groups: First, the very small, frail woman almost a dwarf; second, the woman of normal size, possibly taller than normal, but thin, her limbs and body never having assumed the rounded contour which normally occurs at puberty; third, the large robust woman of somewhat masculine build. Heredity can play no marked role in the cause of this disturbance, since most marked cases are sterile. Sisters may have normal uteri. Acute infection at puberty seems to be the most likely etiological factor, especially in the second type. The first class are sufferers from faulty functioning of the ductless glands.

Cases should be treated with extracts of the thyroid, pituitary and ovarian tissues. Good results are obtained in cases that menstruate infrequently by giving thyroid extract for 2 to 3 weeks, then stopping it and giving ovarian extract for a week. In severe cases the patient should receive two ampules of corpora lutea hypodermically on the day before expected menstruation. If the patient does not menstruate she should be put back on thyroid extract until the following period is expected. After the patient has menstruated a few times the hypodermic injections are withdrawn, but the thyroid and ovarian extracts continued until the habit of menstruation is well established. Dilation, curettage and packing sometimes greatly benefit cases where the lack of development is most evident.—H. W.

Fibroid UTERUS treated by X-rays. Stoney (Florence A.) Brit. Med. J. (Lond.), 1917, **2**, 723.

A married woman aged 42 had a bilobed fibroid of the whole wall, causing discomfort from its size, with constant backache and pressure symptoms. During three months she received eight X-ray treatments, each of two to three pastille doses, filtered. The monthly periods were regular before treatment. Under X-rays she had one heavy followed by two ordinary periods, and they stopped entirely after the sixth treatment.

The fundus was 4¼ inches above the pubes. During treatment it was reduced to 2¾ inches, and three months later was only 2 inches above the pubes. In width the tumor was reduced from over 5 inches to 4 inches during treatment, and since then has become reduced another inch.

The front wall was bulged out so that the distance from pubes to umbilicus was 7¼ inches at first; this has come down to being flat, and now measures 6 inches. Except during the first monthly period, the woman has not been in bed for a day since treatment was begun; she became well and strong and very pleased with the final result. In three other cases similar results were secured; in one the menopause was brought about, but in the other two the periods were only reduced in quantity.

—R. G. H.

(VAGOTONIA) The cause of Addison's disease and scleroderma (Zur Aetiologie der Addisonschen Krankheit und der Sklerodermie.) Gerson (H.), Berl. Klin. Wchnschr., 1918, **55**, 1211.

Gerson reports that people with Addison's disease and with scleroderma exhibit "Vagotonia." The treatment should be directed toward this condition. Diagnosis is easy. People having "vagotonia" are egotists,—hard, rough and impolite,—whereas "sympathicotonics" are sweet in disposition and very polite. (One suspects that this nonsensical article is an intentional satire. If so, it is splendid.)—J. K.

The abstracts in this number have been prepared by the staff assisted by:

E. Hood, New York.
Margaret M. Hoskins, Minneapolis.
L. G. Kilborn, University of Toronto.
E. Novak, Baltimore.
M. M. Portis, Chicago.
J. P. Simonds, Northwestern University, Chicago.
Burton T. Simpson, Buffalo, N. Y.

With the permission of the editors, certain abstracts have been quoted from "Physiological Abstracts," "Chemical Abstracts" and "Surgery, Gynecology and Obstretrics."